AD NUMBER

ADB134687

NEW LIMITATION CHANGE

TO

Approved for public release, distribution unlimited

FROM

Distribution authorized to U.S. Gov't. agencies only; Administrative/Operational Use; 12 Feb 1987. Other requests shall be referred to Commander, U.S. Army Medical Research and Development Command, Ft. Detrick, MD 21701-5012.

AUTHORITY

USAMRDC ltr dtd 29 Jun 1993

DEVELOPMENT OF A SAFE AND EFFECTIVE SKIN DECONTAMINATION SYSTEM: DEMONSTRATION AND VALIDATION

FINAL REPORT

Contract DAMD17-85-C-5200

Richard M. Kopchik, Ph.D.
Principal Investigator

written by:

N. Borenstein, M.S.
D. W. Horsey, Ph.D.
J. H. MacDuff, M.S.
R. B. Steigerwalt, M.S.
H. H. Miller, B.S. (Midwest Research Institute)

February ~~1988~~ 1987

[redacted]

Supported by:

U.S. Army Medical Research and Development Command
Ft. Detrick, Frederick, Maryland 21701

Rohm and Haas Company
Independence Mall West
Philadelphia, PA 19105

ABSTRACT

In the concept exploration/demonstration and validation phase of the Personnel/Casualty Decontamination System Skin Decontamination Kit (PCDS SDK) development program, it was shown that a safe and effective skin decontamination system against chemical warfare (CW) agents can be designed based on Ambergard XE-555 or Ambergard XE-556 resins developed by Rohm and Haas Company. The prototype PCDS SDK developed as part of this contract evolved into a novel soft-pack design. Each PCDS SDK consists of six applications of decontamination material in individual flexible pouches with its own pad for applying, spreading, and removing the decon material. Four thousand prototype PCDS SDK were produced. A Special In-Process Review recommended that the program proceed to full-scale development.

This page is intentionally blank.

SUMMARY

In a previous study, under Contract DAMD17-83-C-3071 with US Army Medical Research and Development Command (USAMRDC), it was shown that it was feasible to design a safe and effective skin decontamination system against chemical warfare (CW) agents with the use of combinations of ion exchange resins and synthetic adsorbents available from Rohm and Haas Company. In the current program, under Contract DAMD17-85-C-5200, the concept exploration/ demonstration and validation phase, the major objectives are:

(1) To reduce the previously identified resin systems to the two best candidates;

(2) To formulate these resins into powders, creams, or pastes without significantly reducing their basic efficacy and safety;

(3) To design and develop practical delivery systems for the formulated decon resins, and to fabricate initial and final experimental prototypes of such systems;

(4) To continue to develop safety data, based on toxicological and human irritation/sensitization data of the formulated products; and

(5) To verify decontamination efficacy of the formulated resin systems via in vitro and in vivo agent testing.

This complex program was organized into six major activities, each with its own sub-objectives and administrative/ funding controls, as follows:

- Application Development and General Support
- Toxicological Studies
- In Vitro Agent Testing
- Packaging Development
- Resin Preparation
- In Vivo Agent Testing

While the Pioneering Applications Research Department of Rohm and Haas has been primarily responsible for the administrative and general support of the technical program, and the Toxicology Department of Rohm and Haas for the toxicology studies, others were subcontracted to perform specific tasks:

- Hill Top Laboratories for human irritation/sensitization studies;
- H. A. Schaeffer as consultant/coordinator of package development;
- Cosmetech Laboratories for formulation work;
- Paco Pharmaceutical Services for package development;

- o Midwest Research Institute (MRI) for in vitro agent testing;
- o Battelle-Medical Research and Evaluation Facility (MREF) for in vivo agent testing (funded directly by USAMRDC, outside the scope of this contract).

Five in vitro physical/chemical tests were developed by Rohm and Haas to establish the base line for the sorptive and reactive properties of the various resin candidates. These tests are:

- o Resin Reactivity (Reactive Capacity)
- o Liquid Sorption
- o Contact Desorption
- o Vapor Sorption
- o Vapor Desorption

These tests were extremely useful for rank ordering the performance of the various resin candidates and in selecting the best two for subsequent formulation into powder, creams and pastes. For example, resin candidates containing Amberlite XAD-16 and Amberlite IRA-400 resin components were eliminated from consideration early in the program based on results of these tests. The number of unformulated candidate systems was thus reduced to Ambergard XE-519 and XE-521 carbonaceous adsorbents. Both of these contain different ratios of the following three components:

- o Amberlite IRA-900(OH) - anion exchange resin
- o Amberlyst XN-1010 - cation exchange resin
- o Ambersorb XE-348F - carbonaceous adsorbent

While the resin selection was based on in vitro tests with simulants (primarily diisopropyl fluorophosphate (DFP) and chloroethyl isobutyl sulfide (CIS)), the same tests were adopted by MRI to verify the resin's efficacy using VX, soman (GD), and mustard (HD). These in vitro tests were also very useful in screening potential excipients to be used as formulating aids in preparation of powders, and aqueous and non-aqueous cream formulations.

After initial screening of many candidate excipient materials, Cosmetech proceeded to develop several versions of the following formulation types in order to achieve the proper balance of performance parameters:

- o Mineral oil-based powders
- * Silicone oil-based powders
- * Hydroxypropyl cellulose, aqueous-based creams
- o Mineral oil-based, non-aqueous creams
- * Silicone oil-based, non-aqueous creams

These various formulated systems were based on Ambergard XE-519 and were tested in in vivo screenings with HD and thickened GD (TGD) by Battelle-MREF. As a result, three formulated systems, designated above by the asterisks, were compounded using Ambergard XE-519 and XE-521 resins as active ingredients. These six formulations (2 resins x 3 types) were prepared in bulk for use in initial experimental prototypes. Subsequent to the preparation of these initial prototypes, and in view of additional feedback from the in vivo tests and the broad temperature requirements established in the Personnel Casualty Decontamination System (PCDS) Joint Service Operational Requirement (JSOR), the only two formulated systems acceptable for final prototype development were the two silicone-oil based powders, designated XE-548 and XE-551. As a result of changes in grinding operations, the formulated powders have been simplified further by eliminating the silicone oil entirely. These final formulated systems, designated Ambergard XE-555 and Ambergard XE-556 resin decontaminants, contain only the active polymeric components (Ambergard XE-519 and Ambergard XE-521 resins, respectively) plus a minor amount of fumed silica for flowability.

Toxicology studies carried out in the previous contract demonstrated that the decon resin systems were safe to use. In this contract, additional toxicological and safety studies have been conducted. These included in vitro and in vivo dermal penetration studies using a ^{14}C-labeled component, acute and sub-acute inhalation (rats), acute toxicity profiles, one generation dermal exposure (rats), and human irritation/ sensitization studies. In the human patch tests, conducted by Hill Top Laboratories, on both unformulated and formulated systems, none of the resins tested showed any evidence indicative of delayed contact sensitization. All results confirm the earlier ones; the resin systems are safe.

At the start of the program, these resin systems were characterized as drugs by the Food and Drug Administration (FDA). Consequently, a petition for exemption for an Investigational New Drug (IND) (#27,295) was jointly submitted to the FDA by Rohm and Haas and the U.S. Army Medical Material Development Activity (USAMMDA) in order to carry out the above-mentioned human safety testing. However, as this project progressed it was evident that characterizing these materials as drugs was burdensome and unnecessary. Thus, in June 1986, a joint petition was submitted to the FDA requesting a release from the drug classification for skin decontaminants. In October 1986 the FDA notified Rohm and Haas that the Ambergard resins (the ingredients for the PCDS SDK) were no longer classified as drugs for Department of Defense (DoD) use.

Extensive in vitro agent testing was conducted by Midwest Research Institute with VX, GD, and HD at various environmental temperatures: 37°C, room temperature, and -35°C. The in vitro agent data have been generated using contact desorption, vapor

desorption, reactivity, and reactive capacity tests on the final formulated products, Ambergard XE-555 and Ambergard XE-556 resins. Generally, the addition of excipients had little effect on test responses. The effect of increasing temperature enhanced resin performance for the reactive tests but may have a slight adverse effect on the contact sorption performance. The data also suggest that the resins perform better against agents than against the corresponding simulants.

Various levels of in vivo testing were carried out by Battelle-MREF in support of this program. Efficacy tests have been conducted on the final formulated products, Ambergard XE-555 and Ambergard XE-556 resins, challenged with GD, TGD, VX, HD, and Lewisite (L). Generally, results indicate that the resin systems are equivalent to the M258A1 for all agents tested except VX. The PCDS SDK prototype provides protection against VX, but not as much as the M258A1.

Six-month storage stability tests on Ambergard XE-555 and Ambergard XE-556 resins have been completed at -18°C, room temperature, 40°C, and 60°C. Storage data are also available on earlier precursors to the active ingredients used in the final products, i.e. Ambersorb XE-519 and XE-521 adsorbents. Although later these materials are somewhat different in moisture content and total reactive sites from the final products, these tests represent the most complete profile to date on storage stability. Based on the vapor desorption test, which measures both sorptive and reactive components of the resins, these precursors have shown no significant losses in sorptive capacities and only minor losses in reactive capabilities, after 11 months' storage at elevated temperatures (up to 60°C). The results are consistent with those observed with XE-555 and XE-556 and suggest that the long range shelf life of the final prototypes may be much better than originally envisioned.

Early concepts of prototype delivery systems consisted of shaker cans or rosin bags for powders, and towelettes or tubes of various kinds for wet formulations. After analyzing their features for the intended application, it was determined that they did not have the desired characteristics and they were discarded as viable candidates. What was desired was a method of delivery which, regardless of formulation, would be simple to use, lightweight, and flexible; could be rapidly deployed; and contained its own applicator.

The design which ultimately evolved as the PCDS SDK prototype was a flexible "soft pack kit" containing no breakable components. Each kit contains six applications of decontamination material in individual flexible, peelable, heat-sealed packets. Each packet contains a non-woven fiberfill pad used for applying, spreading and removing the decon material, designed with flaps for easy opening even by gloved hands. Unlike the M258A1, which requires two separate and sequential applications, a single packet suffices. Furthermore, the PCDS

SDK prototype occupies essentially the same space and weighs less than the M258A1. Preliminary laboratory data suggest that each packet contains sufficient powder to decontaminate a surface of 1300 cm^2. Several thousand PCDS SDK prototypes, each filled with either Ambergard XE-555 or XE-556 resins, were produced at Paco Pharmaceutical Services, utilizing current Good Manufacturing Practices during fabrication.

As described earlier, the sorbent component of the decon resin system is Ambersorb XE-348F carbonaceous adsorbent. This material was produced in a pilot plant located in the Philadelphia plant of Rohm and Haas. The equipment for this pilot plant was government-purchased under the previous contract, but start-up and subsequent product generation occurred in this program. Approximately 3800 pounds of Ambersorb XE-348F adsorbent were manufactured. Numerous mechanical problems were encountered and significant equipment upgrading would be necessary before this facility could generate product on a continuous and efficient basis.

The grinding of resins to the proper particle size has turned out to be far more complex than originally envisioned. Numerous tests at various toll grinding facilities have led to the conclusion that the most feasible equipment for grinding these materials is a mechanical mill whose residence time can be controlled and which does not use air for classification. Jet milling, which had been originally considered the proper approach, turned out to be a totally unacceptable method. A specific mechanical attrition technique has been found and shown to efficiently grind and blend the resin and excipient components in a single processing step. The success of this grinding process resulted in the final simplified formulated system described earlier.

This page is intentionally blank.

FOREWORD

Ambergard, Amberlite, Amberlyst, Ambersorb, and Kydex are trademarks of Rohm and Haas Company, or of its subsidiaries or affiliates. The Company's policy is to register its trademarks where products designated thereby are marketed by the Company, its subsidiaries or affiliates.

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45 CFR 46, and Army Regulation 70-25.

This page is intentionally blank.

TABLE OF CONTENTS

TABLE OF CONTENTS (cont'd.)

TABLE OF CONTENTS (cont'd.)

TABLE OF CONTENTS (cont'd.)

TABLE OF CONTENTS (cont'd.)

This page is intentionally blank.

LIST OF TABLES

LIST OF TABLES (cont'd.)

LIST OF TABLES (cont'd.)

LIST OF TABLES (cont'd.)

LIST OF FIGURES

This page is intentionally blank.

A. NOMENCLATURE

Experimental decontamination resin candidates and systems have been identified throughout this report under various names. The following list describes these materials:

RESIN SYSTEM IDENTIFICATION NUMBERS

Amberlyst XN-1010(H)	Strong Acid Ion Exchange Resin
Amberlite IRA-900(OH)	Strong Base Ion Exchange Resin
Amberlite IRA-400(OH)	Strong Base Ion Exchange Resin
Ambersorb XE-348F	Carbonaceous Sorbent Resin
Amberlite XAD-16	Polymeric Sorbent Resin

XE-517 A two-component resin system consisting of an equimolar (with respect to functional groups) blend of ground Amberlite IRA-900(OH) resin and ground Amberlyst XN-1010(H) resin

XE-518 An aqueous dispersion of XE-517

XE-519 A three-component resin system consisting of one part ground Ambersorb XE-348F resin and two parts of a mixture of ground Amberlite IRA-900(OH) resin and ground Amberlyst XN-1010(H) resin in which the ratio of the functional groups of base resin to acid resin is 1:1

XE-520 An aqueous dispersion of XE-519

XE-521 A three-component resin system consisting of one part ground Ambersorb XE-348F resin and two parts of a mixture of ground Amberlite IRA-900(OH) resin and ground Amberlyst XN-1010(H) resin in which the ratio of the functional groups of base resin to acid resin is 2:1.

XE-522 An aqueous dispersion of XE-521

XE-523 A three-component resin system consisting of one part ground Amberlite XAD-16 resin and two parts of a mixture of ground Amberlite IRA-900(OH) resin and ground Amberlyst XN-1010(H) resin in which the ratio of the functional groups of base resin to acid resin is 1:1

XE-524	An aqueous dispersion of XE-523 containing ethanol as a wetting agent
XE-525	A three-component resin system consisting of one part ground Ambersorb XE-348F resin and two parts of a mixture of ground Amberlite IRA-400(OH) resin and ground Amberlyst XN-1010(H) resin in which the ratio of the functional groups of base resin to acid resin is 1:1
XE-526	An aqueous dispersion of XE-525
XE-527	A two-component resin system consisting of one part ground Ambersorb XE-348F resin and one part ground Amberlite XAD-16 resin
XE-528	An aqueous dispersion of XE-527 containing ethanol as a wetting agent
XE-548	A dry powder formulation of XE-519 containing fumed silica, silicone oil, microcrystaline cellulose, and corn starch to improve flowability
XE-549	An aqueous paste formulation of XE-519 containing hydroxypropyl cellulose and Germaben II preservative (trademark of Sutton Laboratories, Chatham, NJ)
XE-550	A non-aqueous paste formulation of XE-519 containing silicone oil and stearyl alcohol
XE-551	A dry powder formulation of XE-521 containing fumed silica, silicone oil, microcrystaline cellulose, and corn starch to improve flowability
XE-552	An aqueous paste formulation of XE-521 containing hydroxypropyl cellulose and Germaben II preservative (trademark of Sutton Laboratories, Chatham, NJ)
XE-553	A non-aqueous paste formulation of XE-521 containing silicone oil and stearyl alcohol
Ambergard XE-555	A dry powder formulation of XE-519 containing 2% fumed silica
Ambergard XE-556	A dry powder formulation of XE-521 containing 2% fumed silica

Identification of additional samples using Rohm and Haas Laboratory designations or formulated systems using Cosmetech Laboratory designations are tabulated in the 1986 Annual Report on this contract[1].

B. APPLICATION DEVELOPMENT AND GENERAL SUPPORT (ACTIVITY D)

Following is a summary of our objectives, results, and conclusions for most of the experimental work conducted at Rohm and Haas. These efforts have been grouped under five areas; Test Protocol Development, Resin Evaluation and Selection, Formulation Evaluation and Selection, Stability Testing, and Miscellaneous.

1. Test Protocol Development

a. Summary

Probably the best method to demonstrate the efficacy of a skin decontamination system would be extensive in vivo testing using laboratory animals. Such testing would be extremely costly and time-consuming and thus impractical. Therefore, it was important to develop in vitro tests. The in vitro tests were designed to evaluate sorption and destruction of simulants or agents. While in most cases absolute values were not obtained, relative results allowed the ranking of resin systems and potential formulating excipients. An important caveat deserving some emphasis is that the tests were designed to rank resin systems and, therefore, the test conditions may have been extreme. For example, when no significant vapor desorption was seen at room temperature, the test temperature was increased to 37°C in order to force a measurable amount of desorption. It is important to consider the results within the context of the test conditions and objectives.

Five tests were developed to demonstrate the sorptive and reactive properties of the resin system. These tests were designed to allow the ranking of resin systems and formulation excipients.

The tests are:

1. Resin Reactivity (Reactive Capacity)
2. Liquid Sorption
3. Contact Desorption (Liquid Desorption)
4. Static Capacity (Vapor Sorption)
5. Vapor Desorption

b. Results and Discussion

The detailed procedures for these in vitro tests, as well as much of the development/validation efforts, are summarized in the 1986 Annual Report[1]. The test development is outlined briefly below. These tests were utilized by Rohm and Haas for excipient and resin selection as well as by Midwest Research Institute (MRI) for the in vitro agent work.

(1) Resin Reactivity (Reactive Capacity Test) - Because the resin systems are blends of reactive and sorptive resins, it

was desirable to be able to demonstrate the reactive capability of the systems. Studies in the past[2] have demonstrated the ability of functionalized polymers to decompose CW agents utilizing solution phase kinetic techniques. Our objective was to demonstrate the resin reactivity in a more end-use oriented experiment, i.e. neat simulant or agent with dry powdered resin or cream formulations.

The test protocol developed involved mixing the neat simulant with a given quantity of reactive resin and extracting after a set time period with an appropriate solvent. Capillary gas chromatography (GC) analysis of the extract allowed evaluation of the extent of reaction. Diisopropyl fluorophosphate (DFP) was used as a reactive G agent simulant and chloroethyl isobutyl sulfide (CIS) or chloroethyl ethyl sulfide (CEES or half mustard) was used as a reactive mustard simulant.

While the results with the component reactive resins demonstrated the feasibility of the test, a surprising result was found when the test was run on the resin systems containing both reactive and sorptive resins; apparently no destruction takes place. The results show that, when the carbonaceous adsorbent (Ambersorb XE-348F) is present in the decon resins, reaction is essentially nonexistent. This is attributed to the DFP's being irreversibly sorbed onto the Ambersorb XE-348F adsorbent under these conditions; i.e. the DFP is not available to react with the strong base resins.

The test protocol, while useful for the individual reactive resins, does not allow the evaluation of the reactive potential of the resin systems containing both reactive and sorbent resins. (The very strong sorption of the simulants on the carbonaceous adsorbent Ambersorb XE-348F is demonstrated.)

The Reactive Capacity Test reflects changes made to evaluate the reactive potential of the resin systems. The mechanics of the protocol are similar to the Reactivity Test except that an excess of simulant is used and the time before extraction is increased to the point at which essentially all of the functionality on the polymers has reacted to destroy simulant. The reactive capacity is calculated based on the simulant loss.

We were expecting to be able to correlate the reactive capacity with the ionic capacity of the resin systems. That is, if the resin system contained 1.0 meq/g of OH, we might see 0.5 meq/g of DFP destroyed, based on the stoichiometry of the reaction. Unfortunately we did not obtain consistent results from day to day. Replicates on the same day with the same conditions were relatively good but day to day variations were significant. Possible sources of these variations were investigated but never fully resolved. Nevertheless, the test was useful in allowing us to run side by side comparisons of one system to another, i.e. to rank resins.

(2) Liquid Sorption Test - While reactivity is an important criterion for resin selection, the primary mechanism for skin decontamination necessarily will need to be sorptive. Agents must be removed from the skin surface (by favorable partitioning of the agents onto the surface of the resin system) before skin penetration can occur. Various qualitative and semi-quantitative methods exist in the literature for measuring wettability of powders by liquids. A method which has been used to measure both the rate and extent of liquid agent sorption by sorbent powders is based on the Enslinn apparatus[3]. The major drawback of this technique was the fact that the all glass apparatus needed to be cleaned of powders between runs.

Our modified Enslinn apparatus is described in detail in the 1986 Annual Report[1]. The important change is that a removable glass tube is used to contain the powder to be tested. A polyester membrane replaces the glass frit in the original design so that the entire sample tube can be removed. Powder is introduced into the sample tube and placed onto the capillary assembly. The rate of liquid uptake is determined by following the meniscus movement with time.

Simulants were chosen based on their physical properties rather than trying to match chemical functionalities, as properties such as surface tension and viscosity were deemed more important for a Liquid Sorption Test. The physical properties of diethyl malonate (DEM) and methyl salicylate (MS)[4] closely match soman (GD) and mustard (HD), respectively, and were used for this test.

The results can be reported in two ways: the rate (s/mL) or a time to end point (s). The time to end point divided by the volume at the end point was one of the data points used to obtain the rate. A plot of time vs. volume is linear and the two results are essentially equivalent.

Virtually the same ordering of resins was obtained with the HD simulant MS as that obtained with the GD simulant DEM. If the two simulants are accurate simulants for HD and GD, these results indicate that the resin systems which are effective against GD should also be effective against HD. (The MRI agent data reported elsewhere in this report support these results.)

Again, the method is found to be most useful to rank resin systems within a series of runs. Essentially identical data were obtained on the same resin, using the same apparatus by two different operators. However, when this apparatus was broken and replaced by a second apparatus, different rates were obtained. Any ranking of resins needs to be done on the same apparatus under identical conditions. A standard or control sample should be run to verify reproducibility if data from different days' runs are to be compared.

It should be noted that results are not in units that have any real world significance. That is to say that a rate of 600 s/mL does not mean that it would take 10 min to sorb 1 mL off the skin surface. The data are a function of the area of powder in contact with the simulant and does not take into account any mechanical mixing.

(3) Contact Desorption Test (Liquid Desorption) - Another important criterion for a resin-based skin decontamination system is that once an agent is sorbed by a resin it does not come off again. This would be a concern if the contaminated resin were to remain in contact with the skin or to come into contact with unaffected skin. This concern was the basis for development of a liquid desorption test.

The Contact Desorption Test involves mixing a simulant with the resin system and placing the mixture on a piece of M-8 Chemical Agent Detector Paper. (M-8 paper is treated with a combination of dyes that produces an immediate distinctive color change when exposed to a liquid agent. The paper will not detect vapor or extremely small (<50 µL) droplets of agent.) The time to seeing a positive response is noted. Variations in the sensitivity of different lots of M-8 Chemical Agent Detector Paper were noted. This problem was overcome by always running the candidate systems against a control, usually the unformulated resin. Also, attempts were made to use the same lot of M-8 paper for all tests.

DFP and CIS were used as simulants. Reactive simulants were chosen because while reactivity may not be fast enough to serve as the primary skin decon mechanism (relative to sorption), the reactive rate may be fast enough to prevent secondary contamination associated with desorption.

A slight modification in the contact desorption procedure was made late in the program. Discs of M-8 paper were cut to fit into the bottom of a one-ounce vial. The simulant-loaded resin was poured from a test tube onto the paper and the vial was capped. The changes were made to conform with MRI's protocol for agent tests (for direct comparison) and to allow the test to be run at nonambient temperatures in a heating/cooling bath.

(4) Static Capacity Test (Vapor Sorption) - The Static Capacity Test is a standard test for the evaluation of sorbent resins for air filtration. The results are related to the surface area of the resins. An adaptation of the test was incorporated into the current evaluation of skin decon resins in order to evaluate whether fouling of the sorbent resin by formulation excipients occurs.

The test involves placing a sample of resin in a saturated atmosphere of carbon tetrachloride (CCl_4) for 24 hours and measuring the weight gain. During the period of protocol development, three simulants, diisopropylfluoro phosphate (DFP),

dimethyl methyl phosphonate (DMMP) and CCl_4 were studied. In each case the procedure consisted of placing a weighed sample of resin inside a desiccator containing simulant liquid, closing the container and weighing the sample after a measured time period to determine its weight gain (or loss). In some cases a heated container was used in an attempt to speed the attainment of equilibrium.

Effects of bed depth, simulant, and temperature were evaluated during protocol development. Static capacity studies with CCl_4 as a simulant indicated that equilibrium could be reached much quicker, owing to its higher vapor pressure. Unfortunately, it was noted that day to day variability in the values obtained was quite high and that the values were dependent on room temperature variations. In order to control this variable and increase the rate of equilibrium attainment, most CCl_4 static capacities were performed using a heated desiccator at 37°C.

The test method thus decided on was the 24-h CCl_4 Static Capacity. The major drawback of this test is that, if the resin systems contain any significant amount of volatile material (e.g. water), a weight loss due to water vapor desorption may occur concurrent with the weight gain. For this reason, the high moisture containing final resin formulations could not be evaluated with this test. The test was used for initial screening of formulation excipients.

(5) Vapor Desorption Test - Another method for evaluation of the possible secondary contamination from contaminated resin systems is the Vapor Desorption Test. Although the test was designed to look at vapor desorption, it was found to yield much information regarding the sorptive capacity and reactivity of the resins. While this test yields the most information about the resin systems, it is also the most involved and time-consuming.

The test involves passing an air stream over a sample of resin mixed with simulant. The desorbed simulant is collected downstream in a series of bubblers. The resin is extracted to find the amount of simulant retained on the resin. The difference between the simulant quantity used and the sum of the retained simulant and the desorbed resin is reported as "lost" and attributed to reactivity of the resin. The test is generally run at 37°C in order to induce enough desorption so that comparison of the resin systems can be made in a reasonable time period. As in the case for the Liquid Sorption Test, reactive simulants were used. Both destruction and sorption are effective mechanisms to prevent desorption and possible secondary contamination.

- - - - -

In conclusion, five in vitro tests were developed to evaluate and rank polymeric resin systems for reactive and

sorbent properties. The tests are not intended to yield absolute results, but rather to give relative values to allow selection of the best resin systems and formulation excipients.

The Reactive Capacity Test yields a value for the agent decomposition capability of the reactive component of the resin system. The analysis is complicated by the fact that the simulants used in the test are preferentially sorbed onto the sorbent component, and until the sorbent capacity is exceeded destruction does not occur. This makes kinetic measurements difficult.

The Liquid Sorption Test yields a value related to the wettability or gross sorptive action of the resin systems. Although the test does not take into account any mechanical action (mixing due to rubbing), it should be a good measure of the sorptive properties important for skin decon. This test is only applicable to powdered resin systems.

The Contact Desorption Test yields a relative value of the liquid retention properties under static conditions. This could be a very important test when concerned with secondary hazards associated with contaminated resin systems. While some variability is seen, especially near the sorptive threshold of the resins, any large differences in resin would likely be detected.

The Static Capacity Test yields a relative value of the available surface area of the sorptive resin. This test is probably least directly relatable to skin decon efficacy, but should flag any significant fouling of the sorptive resins. The test is applicable only to powdered systems with no significant amount of volatile component.

The Vapor Desorption Test yields not only values for desorption (retention) but also a value for reaction. While the test is not directly related to skin decontamination efficacy, it yields the most information when evaluating the resin characteristics of the overall resin system.

2. Resin Evaluation and Selection

a. Summary

The five tests developed to demonstrate the sorptive and reactive properties of the resin system were used to evaluate four unformulated candidate resin systems. These systems are composed of sorptive and reactive resins. Using these tests, the number of resin systems was reduced from four to two (XE-519 and XE-521).

Six resin systems were developed under a previous contract (DAMD17-83-C-3071), using combinations of sorptive and reactive polymeric resins that were either commercially available or

available in pilot plant quantities. The all-sorptive (XE-527/XE-528) and all-reactive (XE-517/XE-518) systems were dropped from further consideration prior to the start of this contract, leaving four systems to be evaluated. Since it would not be practical to carry these four systems (and possibly three formulations of each) into full development, it was necessary to reduce the number of candidate resins further, based on the in vitro data. The six original resin systems are listed in Table 1.

Table 1

Composition of the Original Six Resin Systems

Resin System			Resin Components	Ratio
A.	XE-517 - Dry Powder		Amberlyst XN-1010(H)	1
	XE-518 - Wet Suspension		Amberlite IRA-900(OH)	1
B.	XE-519 - Dry Powder		Amberlyst XN-1010(H)	1
	XE-520 - Wet Suspension		Amberlite IRA-900(OH)	1
			Ambersorb XE-348F	1
C.	XE-521 - Dry Powder		Amberlyst XN-1010(H)	2
	XE-522 - Wet Suspension		Amberlite IRA-900(OH)	4
			Ambersorb XE-348F	3
D.	XE-523 - Dry Powder		Amberlyst XN-1010(H)	1
	XE-524 - Wet Suspension		Amberlite IRA-900(OH)	1
			Amberlite XAD-16	1
E.	XE-525 - Dry Powder		Amberlyst XN-1010(H)	1
	XE-526 - Wet Suspension		Amberlite IRA-400(OH)	1
			Ambersorb XE-348F	1
F.	XE-527 - Dry Powder		Ambersorb XE-348F	1
	XE-528 - Wet Suspension		Amberlite XAD-16	1

b. Results and Discussion

(1) Selection of Strong Base Resins - The selection of the strong base resin component of the blend was based on the reactivity test. The data in Table 2 clearly demonstrate the faster reaction rate for ground Amberlite IRA-900(OH) resin relative to ground Amberlite IRA-400(OH) resin.

Table 2

Reactivity Test Results for
Ground Amberlite Strong Base Resins with 42.2 mg DFP

Time (min)	% DFP Remaining IRA-900(OH) (10 eq.)	IRA-900(OH) (5 eq.)	IRA-400(OH) (10 eq.)
5	29	78	77
10	14	-	66
15	-	46	-
20	7	-	42
30	5	34	34
45	3	-	24
60	2	16	16
120	-	6	-

This difference in reactivity is further supported by the Vapor Desorption Test results reported in Table 3 and shown in Figure 1. The 18.4% loss was found for the XE-519 (containing Amberlite IRA-900(OH) resin), while only 3.5% loss was found for the XE-525(containing Amberlite IRA-400(OH) resin). The faster rate for the Amberlite IRA-900(OH) resin is likely due to its higher porosity and macroreticular structure and results in a faster penetration rate.

Table 3

Results of Vapor Desorption Experiments
for Decon Resin Systems with 50 microliters of DFP

Resin	Resin Mass(g)	% DFP Desorbed	% DFP Retained	% DFP Lost
XE-517	0.25	18.8	54.1	27.1
XE-519	0.25	11.4	70.2	18.4
XE-521	0.25	15.1	66.7	19.2
XE-523	0.25	10.6	75.4	14.0
XE-525	0.25	24.6	71.9	3.5
XE-527	0.25	4.8	88.1	7.0

Based on these data, the Amberlite IRA-400(OH) resin and hence the XE-525 (and XE-526) were dropped from the program. (It should be noted here that current mechanical grinding techniques

Figure 1

Vapor Desorption Test Results for Initial Six Candidate Resin Systems 0.25 g Resin with 50 µL DFP at 37°C

are resulting in ground Amberlite IRA-900(OH) resin with significantly higher OH content and higher reaction rates.)

(2) Selection of Sorbent Resins - Most of the in vitro tests compared resin systems on a weight basis. The weight comparison is valid only if the densities of the systems are similar. However, the bulk density of Ambersorb XE-348F adsorbent is four times that of Amberlite XAD-16 resin. This results in decon resin XE-519 (1/3 Ambersorb XE-348F) being twice as dense as XE-523 (1/3 XAD-16). Bulk densities of the resin systems and individual components were measured and are reported in Table 4. It is reasonable that the amount of resin in any delivery system will be limited by volume and not by weight.

Table 4

Bulk Densities of Various Resins

Resin System	Measured Density (g/cc)
Amberlite IRA-900	0.50
Amberlite IRA-400	0.63
Amberlite XAD-16	0.10
Ambersorb XE-348F	0.43
Amberlyst XN-1010	0.23
XE-517	0.34
XE-519	0.41
XE-521	0.47
XE-523	0.20
XE-525	0.51
XE-527	0.19

Since an equal volume comparison is more realistic for the decon systems, contact and Vapor Desorption Tests were performed on equal volumes of XE-519 and XE-523, i.e., a weight ratio of 2:1 for XE-519:XE-523. These data are summarized in Tables 5 and 6. These data demonstrate that, on an equal-volume basis, more desorption (contact and vapor) occurs with the Amberlite XAD-16-based resin.

Comparison of static capacity (Table 7) for the two resin systems reveals that the significant advantage of the Amberlite XAD-16-based resin when compared on a volume basis rather than on a weight basis all but disappears.

Table 5

DFP Contact Desorption Comparison
of Equal Volumes of XE-519 and XE-523

DFP Volume (μL)	Resin Weight(g)	Time to Breakthrough (min)
40	0.10g XE-519	1-5
40	0.05g XE-523	1-5
30	0.10g XE-519	10-18
30	0.05g XE-523	5-10
30	0.12g XE-519	>120
30	0.06g XE-523	15-30

Table 6

Vapor Desorption Comparison
of Equal Volumes of XE-519 and XE-523

Resin	XE-519	XE-523
DFP Retained	68%	61%
DFP Desorbed	13%	23%
DFP Lost	19%	16%
CIS Retained	56%	66%
CIS Desorbed	11%	15%
CIS Lost	33%	19%

Table 7

24-hour CCl_4 Static Capacities(mg/g) of Decon Resins

	37°C		Room Temp	
Resin	mg/g	mg/mL[a]	mg/g	mg/mL
XE-519	298	122	632	259
XE-523	475	95	1574	315

a Calculated from bulk densities in Table 4.

Probably the most significant set of data demonstrating the superiority of the Ambersorb XE-348F adsorbent based systems over the Amberlite XAD-16 based resin systems are the Liquid Sorption results. These data are reported in Table 8 and clearly show that the Amberlite XAD-16 resin and Decon Resin XE-523 are difficult to wet.

Table 8

Results of Liquid Sorption Test for Ambersorb XE-348F- vs. Amberlite XAD-16-based Resin Systems

Resin	DEM Uptake Rate (s/mL)x100	95% Confidence Interval	Time to End point(s)	Corr. Coeff.
XE-348F	3.78	3.46- 4.11	15.95	0.991
XE-519	5.53	5.31- 5.75	23.33	0.980
XAD-16	15.36	12.48-18.24	61.78	0.898
XE-523	18.34	16.03-20.65	74.58	0.732

Based on all of these results, XE-523 (and consequently XE-524) was dropped from the program. The two candidate resin systems remaining were Ambergard XE-519 and XE-521 resins. Both of these systems were formulated into final products and delivered in the form of functional prototypes at the end of this contract.

The selection between XE-519 and XE-521 or the formulated versions of these resins (Ambergard XE-555 and Ambergard XE-556 resins, respectively) was not possible, based on any of the in vitro tests performed with simulants at Rohm and Haas or the agent in vitro tests performed at MRI.

3. Formulation Evaluation and Selection

a. Summary

The safety and efficacy of the original six resin systems were demonstrated under the previous contract, DAMD17-83-C-3071. Under the current contract, the materials were to be formulated in such a manner as to prevent significant detrimental effects on the safety and efficacy while improving the physical characteristics of the resin systems. Both dry systems (powders) and wet systems (pastes and/or creams) were developed. The dry systems needed to be formulated for the proper skin adhesion and flow properties. The wet systems needed to be formulated to minimize resin settling. The physical properties were evaluated by a formulation development lab. Efficacy of the formulated resins was evaluated using in vitro and in vivo test methods.

All of the excipients under consideration were FDA Generally Regarded as Safe (GRAS) materials. No safety evaluation of candidate formulations was considered necessary during development. The safety of the final formulations used in the prototypes was later confirmed and is reported in Toxicology (Section D).

A number of candidate laboratories were investigated as formulation development laboratories (FDLs). On the basis of all considerations and site visits, Cosmetech Laboratories, Roselle Park, NJ, was selected. On approval of this sub-contractor by the government, formulation studies utilizing Ambergard XE-519 resin were initiated.

Individual excipients were evaluated first. Some of these, which passed the screening tests, were blended with the resin systems. These blends were then evaluated more extensively. Each of the formulations was narrowed down to one or two powders, aqueous creams, and non-aqueous creams. After further evaluations only powder formulations remained as viable candidates.

b. Results

(1) Evaluation of Individual Excipients - A list of approximately 80 potential formulation excipients was provided to Rohm and Haas by the FDL, Cosmetech Labs. This was reviewed by Rohm and Haas personnel and a number of excipients were eliminated, based on prior knowledge of possible fouling of, or reaction with, the active resin components.

The excipients which remained under consideration were subjected to two quick screening tests to further reduce the numbers. First, these materials were tested for compatibility with M-8 Chemical Agent Detector Paper. Positive responses on the M-8 with the final formulated materials would not be acceptable. Thirty excipients which passed this test were blended with XE-519 at levels ranging from 5% to 10%. Static capacity measurements were then made on these blends to see whether or not any detrimental effects were evident on the sorbent properties of the resins.

In addition to these quick screens, many of these blends were also evaluated, utilizing the Contact Desorption Test and the Liquid Sorption Test. The results of these tests are detailed in the 1986 Annual Report[1] and are not repeated in this document. The FDL was advised as to which excipients were acceptable to be carried into the next stage.

(2) Evaluation of Formulated Resins - Excipients determined to be acceptable in the screening tests were used in various combinations to prepare formulated resin systems. All of the initial formulation work was done with XE-519 (lot CH1811B) owing to its availability.

The objectives were to develop the most suitable products in three categories: powder systems, aqueous creams, non-aqueous ointments, all containing the maximum concentration of active ingredients with a sufficient amount of excipients to provide all properties of pharmaceutically acceptable preparations.

The in vitro evaluation of these initial formulations with simulants was described in the individual monthly reports and will not be repeated in detail here. Relevant data used in the final selection of formulations are discussed below.

(a) Selection of the Aqueous Paste/Cream Formulation - All of the initial six decon resins prepared under the prior contract, DAMD17-83-C-3071, also demonstrated in vivo efficacy as aqueous suspensions. However, these suspensions, ranging in solids content from 15% to 25%, were not stable. After only a few minutes the resin would settle to the bottom leaving free water on top. Therefore, the primary aim in formulating the aqueous creams was to provide a stable suspension. These aqueous systems were difficult to formulate, especially in view of the limited number of suspending and dispersing agents which are compatible with the resins.

Because cellulose derivatives were the most acceptable suspending agents, as indicated by simulant testing, the formulation work was concentrated on these materials. A substantial number of these substances, which are available in a wide range of molecular weights, substitution properties, viscosities, etc., were investigated. The most suitable material was found in hydroxypropyl cellulose, low viscosity. While the formulations, even on reproduction, appeared quite stable initially, bleeding of solvent (water) or syneresis was noted when the products were stored. Concentrations and weight ratios of resin to suspending agent were then adjusted until the most stable system was developed.

In vivo efficacy evaluation of this early aqueous paste formulation (ND0474) under Activity F.2 demonstrated this material to be better than the M258A1 against both TGD and HD (see Section F for results). Although these results were positive, the ND0474 did not perform as well as the unformulated resin (XE-520).

One possible explanation for the lower efficacy of the formulated resin vs. the unformulated suspension was the significant difference in viscosity (ND0474 is a thick paste similar in consistency to petrolatum). For this reason a second aqueous formulation was prepared with a lower viscosity. This lower viscosity material, DWH173, was shown in the in vivo testing to be less effective than the M258A1 against both TGD and HD. Therefore, the low viscosity aqueous cream was dropped from further consideration.

The first formulation, ND0474, was selected as the best aqueous formulation. The initial laboratory designation (ND0474) was assigned an experimental number of XE-549. Similarly, an aqueous formulation of XE-521 was prepared and assigned the experimental number of XE-552.

The formula composition of XE-549 was:

Active resin blend XE-519	26.0%	(by weight)
Hydroxypropyl cellulose	7.3%	
Preservative blend (methylparaben, propylparaben and diazolidinyl urea in propylene glycol (Sutton Lab's Germaben II))	1.0%	
Deionized water	65.7%	

The formula composition of XE-552 was:

Active resin blend XE-521	24.0%
Hydroxypropyl cellulose	4.9%
Preservative blend	1.0%
Deionized water	70.1%

While these aqueous creams were satisfactory from safety and efficacy considerations, they were eventually dropped as viable candidates owing to cold-temperature tests. Initial experimental prototypes (IEPs) were prepared containing XE-549 and XE-552. When these pouches were placed in freezers at -18°C the formulations froze solid and were unusable. As these are temperatures which would reasonably be expected to be encountered under winter climatic conditions, these systems could not be considered for eventual fielding.

(b) Selection of the Nonaqueous Paste/Cream Formulation - Nonaqueous creams and pastes were never felt to have much potential as resin decontaminants. Still there were two reasons for considering these materials. First, a much higher resin content is possible for the non-aqueous formulations than the aqueous formulations. Based on the higher density of the non-aqueous pastes vs. the powders, equal volumes of the pastes and powders would have similar weights of active resin. The second reason was to retain a second option for a wet system in the event the aqueous systems were dropped.

Both mineral oil formulations and silicone oil formulations were prepared. While separation problems were noted for these materials, the in vitro tests did not reveal any strong data for dropping them when compared to XE-520 (the "wet" standard).

Under the first series of in vivo tests, the mineral oil formulation, MAK614, performed very poorly, appearing to spread the HD on the rabbit's back. The silicone oil formulation, DWH174, also performed poorly but demonstrated some efficacy.

The silicone oil formulation, DWH174, was selected as the best non-aqueous formulation. The initial laboratory designation (DWH174) was assigned the experimental number of XE-550. Similarly, a non-aqueous formulation of XE-521 was prepared and assigned the experimental number of XE-553.

The silicone-based ointments (XE-550, XE-553) consisted of:

Active resin blend XE-519 or XE-521	35.0%	(by weight
Dimethyl silicone fluid, 200 cts	58.5%	
Stearyl alcohol	6.5%	

XE-550 was evaluated in the second series of in vivo tests because of the possibility that this formulation may have performed as well as the M258A1 under the more realistic application conditions used in these tests. The data (see Section F) show that XE-550 still performed very poorly against TGD, HD and VX. Therefore, the non-aqueous creams were also dropped from further consideration.

One additional reason for dropping both the aqueous and non-aqueous pastes should be noted. Preliminary area coverage determinations, from evaluations both of resin spreading and of simulant removal, were inferior for the creams relative to the powders.

(c) Selection of the Powdered Formulation - Since the active ingredient of the resin based decon systems are finely ground resins, the powdered systems required the least amount of formulation. Formulating was necessary to improve flowability and skin adhesion and to reduce dusting.

It was found that the factors of skin adherence/dust reduction were optimized with low concentrations of mineral oil and modified maize starch. Two formulations eventually evolved from this early work. Both contained maize starch, fumed silica, and microcrystalline cellulose. The formulations, EOJ3556 and ND0472, differed in containing either mineral oil or silicone oil, respectively. In vitro evaluation of these materials did not indicate any significant decrease in efficacy.

Both of these resins were submitted to Battelle-MREF for in vivo agent screening tests (see in vivo testing section for results). Both of the formulations tested "as good as or better than the M258A1" against TGD in the in vivo tests. Only the EOJ3556 (mineral oil) formulation was tested against HD in the early in vivo screen. This formulation was found to be worse than the M258A1. As will be discussed below, the mineral oil cream formulation was significantly worse than the silicone oil cream formulation. Thus, it was assumed that mineral oil has a greater detrimental effect on the efficacy against HD, and the

ND0472 would have performed better than the EOJ3556 against HD had it been tested.

The silicone oil formulation was therefore selected as the best powder. The initial laboratory designation (ND0472) was assigned an experimental number of XE-548. Similarly, a dry powder formulation of XE-521 was prepared and assigned an experimental number of XE-551. The efficacy of the XE-548 against HD was demonstrated in a second series of in vivo tests by Battelle-MREF.

The formula compositions of XE-548 and XE-551 were:

Active resin blend XE-519 or XE-521		86.0% (by weight)
Microcrystalline cellulose		8.0%
Function:	particle divider, "glidant" (flow promoter)	
Fumed silica		2.0%
Function:	anti-caking agent, coats particles due to extremely high surface area	
Dimethyl polysiloxane		2.0%
Function:	promotes good skin adherence, reduces moisture uptake due to hydrophobic character	
Modified (etherified) cornstarch		2.0%
Function:	works in synergism with micro-cryst. cellulose to enhance flow	

Unformulated XE-519 was also evaluated as a candidate powder decon material in the second series of in vivo testing by Battelle-MREF. While both the XE-548 and XE-519 performed as well as, or better than, the M258A1 against TGD and HD, only the XE-519 demonstrated any efficacy against VX (see Section F). These results suggested that minimization of formulation excipients would be beneficial.

Concurrently with activity in this area, new grinding techniques were being evaluated. As discussed in the Resin Preparation (Section G), several advantages in using mechanical grinding techniques over the previously used air impact techniques were evident. One consequence of the new grinding technique was a significantly higher moisture content of the ground resins. It had already been demonstrated that water in these resin systems did not adversely affect the in vivo efficacy of the resins. The amount of moisture was not enough to make the resins wet or paste-like, but was enough to reduce the dusting. Cosmetech Laboratories developed two final formulated powder resin systems which eliminated the need for the flow enhancer, the glidant, and the adherence promoter. The only excipient which was retained in the formulation was fumed silica, the anti-caking agent. However, its level was significantly reduced. Consequently, the active resin composition was increased from 86% to 98% by weight.

These final formulated powders were given the following designation:

Ambergard XE-555 Resin:

Active resin blend XE-519	98.0% (by weight)
Fumed silica	2.0%
Function: anti-caking agent, coats particles due to extremely high surface area	

Ambergard XE-556 Resin:

Active resin blend XE-521	98.0% (by weight)
Fumed silica	2.0%

Given more time some additional fine tuning of the powder formulations would no doubt be possible, and perhaps preferable. These two formulations were the final materials selected for use in the final PCDS SDK prototypes delivered to U.S. Army Medical Materiel Development Activity (USAMMDA) at the conclusion of this contract. These were also the materials that were evaluated in the in vivo definitive efficacy testing.

4. Stability Testing

a. Summary

Stability testing was initiated on the ground Amberlite IRA-900(OH) resin and on the unformulated resin systems XE-519 and XE-521. Samples of bulk materials were stored at room temperature, 40°C, and 60°C. All of the resins used were ground under the previous contract, DAMD17-83-C-3071. These materials were stored at room temperature as ground resins for approximately 1 year prior to initiation of these tests. Stability testing on the final resin formulations, Ambergard XE-555 and Ambergard XE-556, was initiated when the prototypes were produced. This testing began late in the contract and only 6-month results are available. Stability testing for package integrity was also initiated on the final PCDS SDK (advanced development) prototypes. Inital microbial contamination studies of Ambergard XE-556 and packet integrity studies are both reassuring.

b. Results

(1) Strong Base Resin Stability - Of the three components of the resin systems, only the strong base resin is believed to have any significant long-term stability problems. While the chloride forms of the quaternary amines are very stable, the hydroxide forms are less stable at high temperatures. Two mechanisms for the decomposition of the strong base Amberlite IRA-900(OH) resin are known: Hoffman degradation, resulting in

loss of trimethyl amine or methanol[5], and/or reaction with atmospheric CO_2, resulting in conversion from the OH^- form to the HCO_3^- form.

Elevated Temperature Stability Testing was initiated on the available ground Amberlite IRA-900(OH) resin. Since we did not want to wait long into the contract to begin the studies, available resin, already approximately 50% in the HCO_3^- form, was used. While this material is not truly representative (lower activity) of the Amberlite IRA-900(OH) resin that will be used in the final resin systems, it was the only material that was available in sufficient quantity for the stability tests. (The high conversion of OH^- to HCO_3^- in this material was likely due to early grinding conditions and not due to storage stability.)

The samples were analyzed for the percentage of extractables, percentage of solids, static capacity, and reactivity. The results were detailed in the 1986 Annual Report[1]. Only the reactivity test showed any significant change over more than 1 year of testing. The reactivity results are reported in Table 9. The reactivity for the 60°C storage samples is essentially nonexistent at this time.

Table 9

Storage Stability Data for Ground Amberlite IRA-900(OH) Resin

Time, days	Approx. Months	Reactivity, % DFP Destroyed[a] 25°C	40°C	60°C
0	0	91%	91%	91%
35	1	86%	86%	64%
75	2	89%	83%	42%
104	3	83%	76%	10%
125	4	81%	75%	21%
257	9	62%	52%	4%
378	12	59%	47%	4%
451	15	58%	62%	7%

[a] % DFP (40.0 microliters) destroyed after 30 min with 1.0 g resin.

The reactivity results reflect the change in functionality. The only significantly reactive form of the resin is the OH^- form. Therefore, either decomposition mode would result in reactivity loss.

(2) XE-519 and XE-521 Storage Stability - The accelerated storage stability testing was initiated on resin blends XE-519 and XE-521 in January 1986 when these systems were identified as the most promising candidate systems of the initial six. These resins were ground and blended under contract DAMD17-83-C-3071 in

July 1984. The time zero in the following tables actually represents 18 months of storage under ambient conditions. The results are shown in Tables 10 and 11.

Table 10

Storage Stability Data for XE-519
(Component of Ambergard XE-555 Resin)

Time, months	Temp, °C	Extractables %	Solids %	Static Capacity CCl_4 mg/g	Reactive Capacity DFP meq/g
0[a]	25	0.10	89.5	340.5	0.320
1	25	0.01	90.0	343.5	-
2	25	0.01	90.5	323.0	0.150
3	25	0.01	86.5	223.0	0.305
6	25	-	-	311.0	0.550
9	25	0.01	-	255.0	0.410
1	40	0.01	90.5	338.0	-
2	40	0.01	90.0	345.0	0.190
3	40	0.01	94.0	265.5	0.320
6	40	-	-	346.5	0.340
9	40	0.01	-	275.0	0.425
1	60	0.01	94.5	351.0	-
2	60	0.01	94.5	370.0	0.300
3	60	0.01	96.5	284.0	0.165
6	60	-	-	371.5	0.265
9	60	0.01	-	383.0	0.125

[a] At initiation of accelerated tests, the resins were 18 months old.

The Static Capacity Test is related to the sorbent capacity of the resin systems and is a control on the sorbent component just as the Reactive Capacity Test is a control on the reactive component. The efficacy of the resin system is primarily attributed to the rapid removal of agents from the skin surface (sorption). Destruction of the agents is an important secondary process. No decomposition of the sorptive resins under very long storage conditions would be expected. Some thermal decomposition of the reactive resin will occur with time, but a corresponding loss of efficacy may not occur. Accelerated stability testing of the component resins still shows significant reactivity after 9 months at temperatures up to 60°C (140°F).

Table 11

Storage Stability Data for XE-521
(Component of Ambergard XE-556 Resin)

Time, months	Temp, °C	Extractables %	Solids %	Static Capacity CCl_4 mg/g	Reactive Capacity DFP meq/g
0[a]	25	0.01	89.0	283.5	-
1	25	0.01	90.0	296.0	-
2	25	0.01	88.5	295.5	0.240
3	25	0.01	89.0	255.0	0.345
6	25	-	-	259.5	0.505
9	25	0.01	-	198.0	0.385
1	40	0.01	91.0	320.0	-
2	40	0.01	92.0	338.0	0.220
3	40	0.01	92.5	265.5	0.245
6	40	-	-	319.0	0.390
9	40	0.01	-	299.0	0.145
1	60	0.01	93.5	310.0	-
2	60	0.01	94.0	312.5	0.265
3	60	0.01	99.5	327.0	0.055
6	60	-	-	370.5	0.165
9	60	0.01	-	297.0	0.130

[a] At initiation of accelerated tests, the resins were 18 months old.

As mentioned in Subsection B.1, Protocol Development, one of the best tests for resin evaluation is the Vapor Desorption Test. This test is prohibitively time-consuming for routine analysis of storage stability samples. However, as a one-time evaluation, samples stored in the various temperature environments for approximately 11 months (324 days) were evaluated in these tests. The results are summarized in Tables 12 and 13 and in Figures 2 and 3. The standard deviations shown in the tables are greater than desired, but some trends are noted. The results are interesting in that the amount of DFP desorbed actually decreases after storage at elevated temperatures. This is a desirable although unexpected result. The CIS results do not show this decrease in desorption, but neither do they show an increase. These data suggest that storage at elevated temperatures does not have a detrimental effect on the sorptive properties of the resin. A slight decrease in the percentage lost after storage at elevated temperature may be indicative of the expected thermal loss of strong base functionality in the resin systems. All of these tests were run with 0.17 g of resin and 50 microliters of DFP or

Table 12

Vapor Desorption Results on Storage Stability Samples with DFP as Simulant (after 11 mo. Storage)

Resin	Storage Temp.	% Desorbed	Std Dev	% Retained	Std Dev	% Lost	Std Dev
XE-519	RT	29.6	9.3	52.1	11.3	18.3	3.1
XE-519	40°C	18.9	6.0	62.3	5.2	18.8	0.9
XE-519	60°C	18.3	2.9	69.5	2.1	12.2	2.0
XE-521	RT	41.0	7.0	39.2	5.5	19.8	2.1
XE-521	40°C	28.5	3.8	57.4	1.4	14.1	2.6
XE-521	60°C	21.6	6.7	64.2	5.8	14.2	3.6

Table 13

Vapor Desorption Results on Storage Stability Samples with CIS as Simulant (after 11 mo. Storage)

Resin	Storage Temp.	% Desorbed	Std Dev	% Retained	Std Dev	% Lost	Std Dev
XE-519	RT	18.8	6.6	51.3	6.9	29.9	0.3
XE-519	40°C	17.0	0.8	48.2	1.3	34.7	0.6
XE-519	60°C	17.0	4.7	55.0	2.6	28.0	2.1
XE-521	RT	21.5	1.1	50.9	2.1	27.6	3.2
XE-521	40°C	19.2	2.8	52.2	1.7	28.6	4.5
XE-521	60°C	19.8	0.2	62.5	6.4	17.6	6.2

Figure 2

Vapor Desorption Test Results
Comparison of Storage Stability Samples
with DFP as Simulant

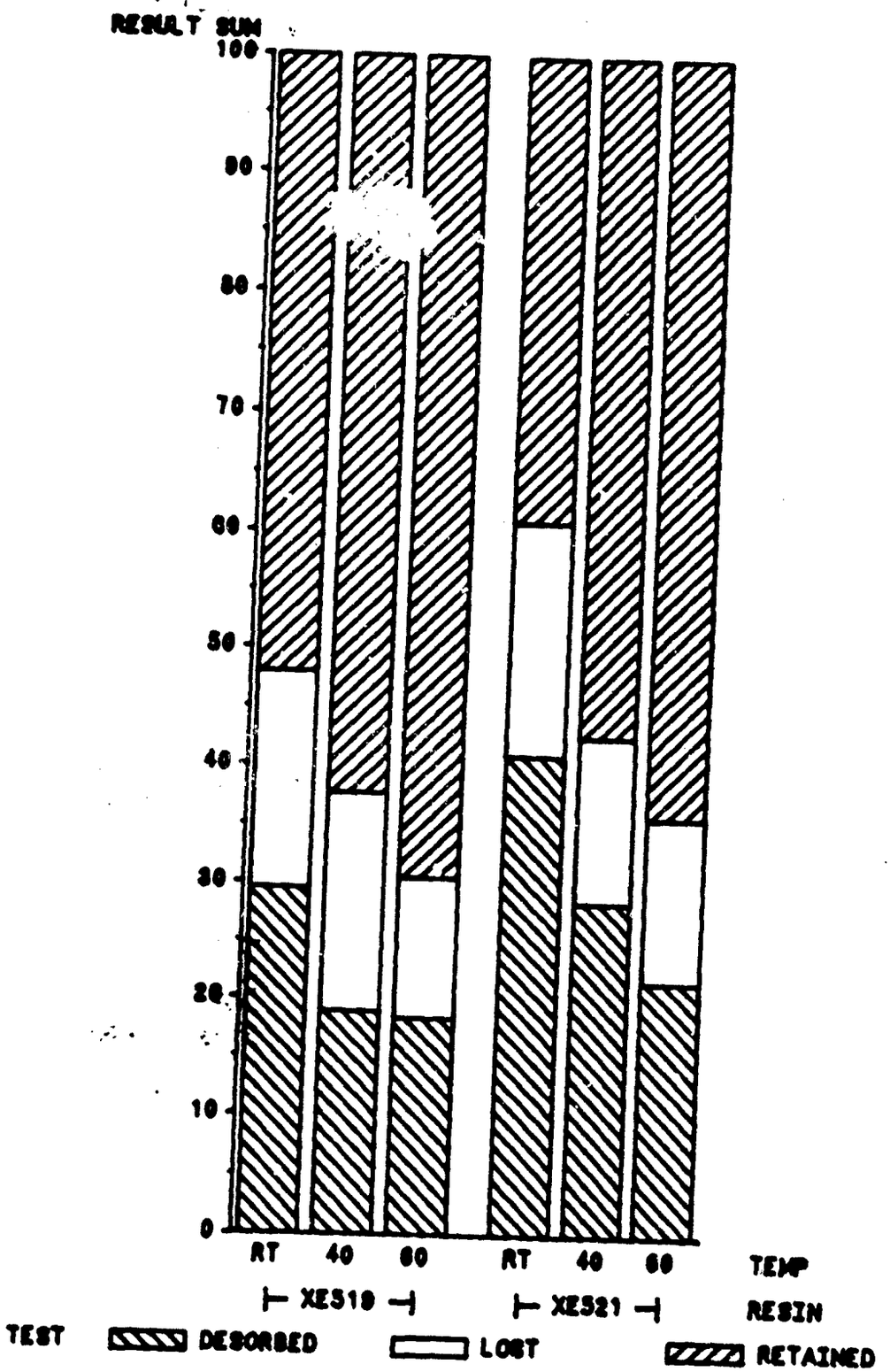
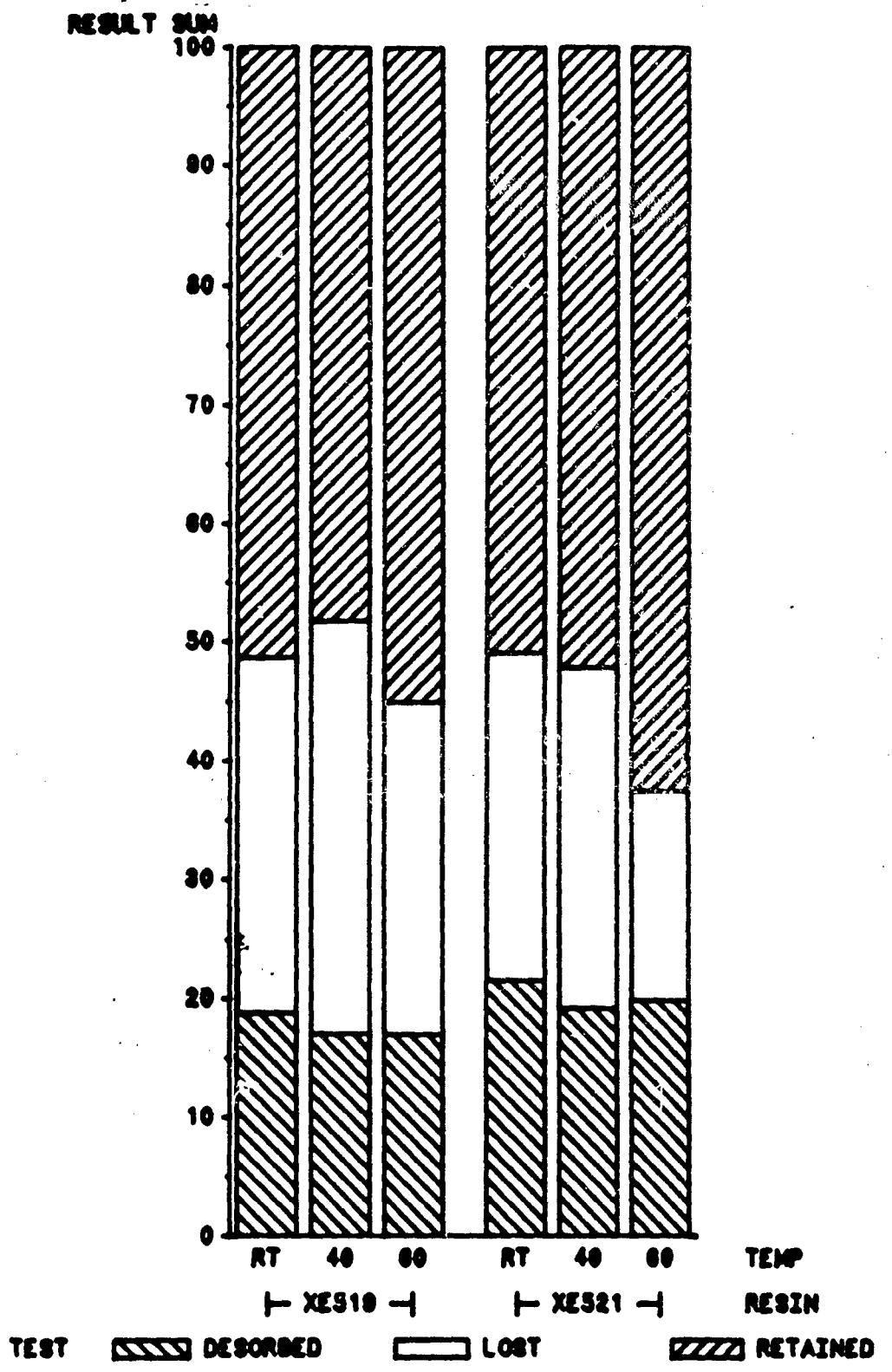


Figure 3

Vapor Desorption Test Results
Comparison of Storage Stability Samples
with CIS as Simulant



CIS. Zero-time data under these test conditions were not available. Comparison of current data (11 months' storage at room temperature) with data generated early in the program at slightly higher resin levels show no significant change in sorptive or reactive properties.

(3) Advanced Development Prototype Storage Stability - Ambergard XE-555 and Ambergard XE-556 Resins - Long-term storage stability and shelf life determinations on the final formulations, Ambergard XE-555 and Ambergard XE-556 resins, are continuing under contract DAMD17-87-C-7116. Current grinding techniques will result in a much higher initial hydroxide content (related to the reactivity) in the reactive resins. Storage stability testing of the advanced development prototypes for package integrity was also initiated. Storage conditions for all of these test include -18°C, room temperature, 40°C, and 60°C environments.

Six-month results obtained in accelerated storage stability testing of Ambergard XE-555 and Ambergard XE-556 resins are shown in Tables 14 and 15, respectively. These are the same lots of material used in the final prototypes. Four storage conditions are being utilized. In addition to the room temperature, 40°C, and 60°C conditions, samples have been placed in a freezer at -18°C (0°F).

Inspection of the data does not reveal any striking changes during the first 6 months of stability testing. Some slight changes in stability test results are evident, as a function of either time or temperature. In order to test the significance of the changes with time or temperature, a regression analysis was run on most stability tests as a function of time (days) or temperature.

The percent extractables increased slightly with time. The values are, even at 6 months, too low to be of concern. The percent solids were run as a control on any drying that may have occurred, resulting in a artificially high result in another test. As most tests are run on a weight basis, a dry sample would have more active resin than a sample containing water. For this reason, the acidity and basicity were divided by the solids prior to the regression analysis. Also, in the ratio of basicity to acidity, any moisture/solids differences would be canceled. The regression analysis data (not shown) indicates a slight decrease in the corrected basicity as a function of temperature, and a corresponding decrease in the ratio. This decrease is expected because of thermal decomposition of the strong base resin. No significant change in the Reactive Capacity Test is seen, indicating that the loss of strong base functionality is not large. Although a lot of variability is seen in the Kinetic Iodine Test, no significant increase in UV absorbance (which would indicate a decrease in the available surface area of the resin) is seen.

Table 14

Accelerated Storage Stability Results on Ambergard XE-555
Lot EOJ3936

Time, days	Temp, °C	Extractables, %	Solids, %	Acidity, meq/g	Basicity, meq/g	B/A[a] Ratio	Kin I UV Abs[b]	Reactive Capacity, meq/g
0	25	0.02	71.2	0.69	0.65	0.95	0.51	ND[c]
34	-18	0.00	75.7	0.74	0.64	0.87	0.66	0.73
34	25	0.00	74.8	0.72	0.63	0.87	0.62	0.74
34	40	0.00	75.5	0.75	0.62	0.83	0.68	0.73
34	60	0.03	77.2	0.74	0.59	0.80	0.63	0.71
63	-18	0.00	70.4	0.64	0.60	0.95	0.62	0.89
63	25	0.00	71.0	0.62	0.60	0.96	0.66	0.96
63	40	0.00	71.9	0.67	0.58	0.86	0.59	0.95
63	60	0.00	73.3	0.81	0.52	0.64	0.80	0.95
96	-18	0.00	70.6	0.66	0.64	0.96	0.61	0.74
96	25	0.02	70.6	0.68	0.60	0.88	0.57	0.79
96	40	0.02	77.1	0.70	0.61	0.87	0.53	0.79
96	60	0.05	73.3	0.94	0.55	0.59	0.38	0.91
153	-18	0.09	70.6	0.70	0.60	0.86	0.35	0.90
153	25	0.04	71.5	0.71	0.53	0.75	0.30	0.86
153	40	0.03	74.1	0.77	0.51	0.66	0.32	0.83
153	60	0.06	73.2	0.87	0.45	0.52	0.48	0.91
182	-18	0.02	71.5	0.71	0.62	0.87	0.56	0.92
182	25	0.00	72.1	0.73	0.61	0.84	0.46	0.78
182	40	0.02	75.5	0.79	0.60	0.75	0.73	0.77
182	60	0.08	83.1	0.93	0.59	0.63	0.59	0.67

[a] B/A = Basicity/Acidity
[b] Kin I UV Abs = Kinetic Iodine Ultraviolet Absorbance
[c] ND = no data

Table 15

Accelerated Storage Stability Results on Ambergard XE-556
Lot EOJ3937

Time, days	Temp, °C	Extractables, %	Solids, %	Acidity, meq/g	Basicity, meq/g	B/A Ratio	Kin I UV Abs	Reactive Capacity, meq/g
0	25	0.01	64.2	0.40	0.79	1.97	ND	ND
34	-18	0.01	66.2	0.43	0.77	1.78	0.72	0.38
34	25	0.01	67.6	0.42	0.77	1.83	0.71	0.31
34	40	0.01	65.8	0.43	0.74	1.70	0.92	0.45
34	60	0.01	68.1	0.44	0.73	1.64	1.22	0.39
63	-18	0.03	65.1	0.37	0.78	2.09	0.75	0.78
63	25	0.02	65.6	0.34	0.73	2.15	0.63	0.74
63	40	0.03	65.3	0.31	0.71	2.27	0.84	0.73
63	60	0.05	66.6	0.38	0.68	1.80	0.82	0.70
96	-18	0.00	65.7	0.33	0.74	2.26	0.80	0.67
96	25	0.03	66.1	0.36	0.72	1.99	0.74	0.58
96	40	0.02	67.5	0.41	0.72	1.76	0.82	0.67
96	60	0.09	65.3	0.49	0.71	1.43	1.00	0.53
153	-18	0.00	65.1	0.43	0.61	1.43	0.24	0.79
153	25	0.01	64.5	0.39	0.58	1.48	0.28	0.66
153	40	0.02	65.0	0.47	0.58	1.22	0.59	0.63
153	60	0.07	64.8	0.46	0.60	1.29	0.60	0.61
182	-18	0.08	67.0	0.44	0.75	1.72	0.55	0.76
182	25	0.00	65.1	0.39	0.77	1.95	0.70	0.51
182	40	0.02	63.5	0.49	0.74	1.49	0.82	0.58
182	60	0.04	64.9	0.45	0.73	1.62	0.98	0.62

(4) Microbial Contamination on Ambergard XE-556 Resin - An investigation of the Ambergard XE-556 resin for microbial contamination was conducted in order to determine whether or not it would be necessary to monitor bacteria as part of future stability/shelf-life testing, or possibly include a bactericide in the resin system formulation.

Samples of Ambergard XE-556 resin from both bulk containers and prototype packets were diluted in buffer and plated on agars which promote both bacterial and fungal growth. Also, resin samples were placed on the surface of each of the culture media. Only trace fungal and bacterial growth was detected after 8 days. The traces of growth detected were most likely a result of air contamination during sample preparation. There is no indication that the resin will support microbial growth in the skin decontamination kits. Therefore, it is not

considered necessary to monitor microbial growth as part of the stability testing.

(5) Packet Integrity - Storage stability testing of prototype kits containing Ambergard XE-556 was initiated on 15 December 1986. Four storage conditions are being utilized: -18°C (0°F), room temperature, 40°C, and 60°C. Three months of testing are now complete. The tests are intended to investigate packet integrity, not resin stability.

Solids were run on the resin beginning at month 2. A drying of the resins would be expected if leaks were present (at the elevated temperatures). Two leak tests were conducted. The PACO leak test is the quality control (Q.C.) test used by PACO during production of the packets. It involves subjecting the packets to a vacuum of 25 in. Hg for 15 s. The packets pass if they inflate but do not burst or expel any powder. The ASTM leak test (ASTM D3078-84, Standard Test Method for Leaks in Heat Sealed Flexible Packages) involves submersing the packets in water and then subjecting the packets to a vacuum of 15 in. Hg for 30 s. The packets pass if no bubbles are seen and/or the resin is not found to be wet upon opening the packets. The packets were examined for delamination, holes, cracking, discoloration, and any other visible deformation. All tests were run in duplicate. As some of the tests are destructive, all tests for a particular time and temperature were not run on the same packet. The results are shown Table 16.

No changes were observed in the physical examination. A significant number of packets were observed to leak using the ASTM method. As this is more stringent than the method used for Q.C. at PACO during production of the packets, it is difficult to know whether or not failures are due to exposure at the various environments, or whether or not a significant number of packets would have failed as produced. Changes in packet construction are expected in the full-scale development. The next testing is scheduled at 6 months.

5. Miscellaneous Testing

Included in this section are brief summaries of work performed under Activity D that do not fall under the first four subsections of this section of the report. Much of the experimental data are reported in the 1986 Annual Report[1] and are not repeated here.

a. Near Infrared Signatures for Decon Resins

The spectral reflectance results on the final decon formulations as well as those on some of the early candidate systems and component resins were provided by the Materials, Fuels and Lubricants Laboratory at Belvoir Research, Development and Engineering Center (BRDEC), Ft. Belvoir, VA. BRDEC reports nothing unusual about the reflectance spectra of these powders.

They are "typical of black or near-black pigments producing a flat curve from 380 to 1000 nm." This demonstrates the essentially nonreflective nature of the resins and the flatness of the spectra; i.e. no strong absorptions were present in the spectral region of interest.

Table 16

Ambergard XE-556 Resin -
Prototype Packet Stability Testing

Day	Temp, °C	Run No.	Solids, %	PACO Leak	ASTM Leak	Physical Exam
34	-18	1	-		Passed	Passed
34	-18	2	-		Passed	Passed
34	25	1	-		Passed	Passed
34	25	2	-		Passed	Passed
34	40	1	-		Passed	Passed
34	40	2	-		Passed	Passed
34	60	1	-		Passed	Passed
34	60	2	-		SLLK-NM[a]	Passed
61	-18	1	75.8	Passed	Passed	Passed
61	-18	2	73.7	Passed	SLLK-NM	Passed
61	25	1	70.6	Passed	Passed	Passed
61	25	2	72.3	Passed	SLLK-NM	Passed
61	40	1	78.4	Passed	Passed	Passed
61	40	2	80.6	Passed	Passed	Passed
61	60	1	84.7	Passed	Passed	Passed
61	60	2	93.5	Passed	SLLK-NM	Passed
86	-18	1	73.2	Passed	SLLK-NM	Passed
86	-18	2	72.4	Passed	SLLK-WT	Passed
86	25	1	75.0	Passed	Passed	Passed
86	25	2	75.2	Passed	SLLK-NM	Passed
86	40	1	93.0	Passed	LK-WT[b]	Passed
86	40	2	84.3	Passed	SLLK-NM	Passed
86	60	1	94.9	Passed	LK-WT	Passed
86	60	2	92.1	Passed	Passed	Passed

[a] SLLK-NM = slow leak, no moisture in packet
[b] LK-WT = leaked, wet inside packet

b. Effects of Resins on Chemical Protective Clothing

The objective of this activity was to provide a quick screen to evaluate any detrimental effect that the resin systems may have had on the properties of chemical protective garments. The garment tested was an OG84 supplied by USAMMDA.

Three types of standard garment tests were conducted under this activity. A Vapor Contamination/Vapor Penetration Test and two Liquid Contamination/Liquid Penetration Tests[6]. Both DFP and CIS were used as simulants.

The first of the two liquid penetration tests was the Mandril Test. This test simulates the liquid penetration that could occur on those areas of the clothing that could be under tension (held tightly against the body) when the liquid droplets strike the clothing. The second test was the Expulsion Test. This test simulates the liquid penetration that could occur on those areas of the clothing where, after the droplet hits the clothing, an external force is applied to the contaminated area.

The Mandril and Expulsion Tests were conducted on garments that were exposed to powder, aqueous pastes, and non-aqueous pastes. A factorial design approach was used to evaluate all of the factors of interest without having a prohibitively large number of samples. There were no observed detrimental effects for any of the skin decon resin formulations. While it is likely that the resins could improve the chemical protective properties of the garment, this could not be demonstrated with this pass/fail type of test.

The Vapor Contamination/Vapor Penetration Test involved using a 2-in.-diameter fabric sample in a Dawson cup. A simulant vapor stream was passed through the sample at a flow rate of 300 mL/min. A capacity is calculated from the break time. Only garments exposed to the final formulations (powders) were used in these tests. The data yield no evidence of any detrimental effect of the resin on the protective properties of the fabric. An actual increase in capacity is seen, but the increase in not statistically significant.

c. Area Coverage

Area coverage data for individual PCDS SDK prototype packets, generated using rough Kydex plastic surfaces and thickened methyl salicylate (TMS) as a simulant, meet or exceed the area coverage requirement specified in the JSOR. The requirement is for a minimum of three decontaminations of an area of 1300 cm^2 at a challenge level of 2.5 g/m^2 agent (simulant) for each packet. These requirements are based on an exposed skin area of a soldier estimated by the government to be 1300 cm^2.

The experiment involved distributing the TMS over the area of interest in approximately 10-mg drops. The surface was rubbed for 2 min with a prototype packet. The excess resin was removed and the surface washed with alcohol. The alcohol washings were analyzed for remaining simulant. The experimental results, summarized in Table 17, show that, even at 2600 cm^2 area, 97% removal is achieved. These results were obtained under controlled laboratory conditions, and some decrease in area coverage may be expected under field conditions. These tests

suggest that one packet should decontaminate the required 1300 cm^2 area. A single experiment using a package maintained at -70°C until immediately prior to the decontamination procedure was conducted. No significant loss of efficacy was evident. The PCDS SDK prototypes contain six individual decontamination applications, twice as many as in the M258A1 kit.

Table 17

Area Coverage Data Using Synthetic Surfaces and Simulants

Resin	Area cm^2	Challenge g/m^2	Wt. TMS mg	Remaining mg TMS	Removal
XE-548	1300	2.5	325	9.4	97%
XE-548	2600	2.5	650	10.9	97%
XE-548	5200	2.5	1300	176	86%
XE-548	650	10.0	650	1.2	99%
XE-548	1300	10.0	1300	7.7	99%
XE-551	1300	2.5	325	7.5	98%
XE-551	1300	2.5	325	6.1	98%
XE-551	1300	2.5	325	.7	99%
XE-555	1300	2.5	325	2.3	99%
XE-556[a]	1300	2.5	325	1.1	99%

[a] Decon packet was maintained at -70°C for 5 days prior to application. The surface was at room temperature.

Additionally, in vivo data conducted at Battelle-MREF can be extrapolated to support the in vitro area coverage data. Efficacy for 150 mg of powdered decon resins was demonstrated in the initial in vivo experiments using 2- to 4-kg rabbits challenged with 5.65 mg TGD per kg rabbit (11.3-22.6 mg/rabbit). If 150 mg resin decontaminated at least 11.3 to 22.6 mg TGD then 2.8 g resin should decon at least 211 to 422 mg of TGD. At a threat concentration of 2.5 g/m^2 one packet (2.8 g) will therefore decon at least 840 to 1680 cm^2 area.

d. Low Temperature Studies

Formulated and unformulated resins were subjected to freezing temperatures to evaluate their usefulness under cold climatic conditions. Bulk materials and initial experimental prototypes (IEP) were evaluated after 16 hours in a freezer thermostated at -18°C (0°F). The subjective results are summarized below.

Unformulated Powder
XE-521 Bulk - Still free-flowing.

Formulated Powders
XE-551 Bulk - Still free-flowing.
XE-548 IEP - Still free-flowing. Good spreading on plastic surface.

Formulated Aqueous Creams
XE-552 Bulk - Frozen solid.
XE-549 IEP - Frozen solid. Unable to spread on plastic surface.

Formulated Silicone Oil Creams
XE-553 Bulk - Viscous, not frozen.
XE-550 IEP - Viscous, not frozen. Poor spreading on plastic surface, but may be due to formulation and not cold.

e. Effects of Environmental Interferences

(1) Temperature Effects - Some limited temperature effect data was reported in the 1986 Annual Report[1]. More extensive testing has been performed on the final formulations. These results are detailed in Section E where agent/simulant comparisons were made.

(2) Synthetic Sweat - The Contact Desorption Test and Reactive Capacity Tests were run using DFP and CIS on XE-519 with synthetic sweat (approximately 10% of the resin weight). The amount of simulant used was at approximate use levels. The tests results indicate that at the levels investigated there were no detrimental effects with the sweat.

(3) Effects of Diesel Fuel on Reactive Capacity - The Reactive Capacity Test was run on XE-519 contaminated with diesel fuel. This was done either by mixing the XE-519 with the diesel fuel, followed by DFP addition, or by mixing the XE-519 with DFP, followed by diesel fuel addition. These results, summarized in Table 18, indicate no significant detrimental effects.

Table 18

Effects of Diesel Fuel on Reactive Capacity of XE-519

Wt. XE-519	µL Diesel Fuel	Order of Addition	Reactive Capacity
0.1 g	0	XE-519 + DFP	0.25 meq/g
0.1 g	10	XE-519 + DFP + Fuel	0.22 meq/g
0.1 g	10	XE-519 + Fuel + DFP	0.23 meq/g
0.1 g	50	XE-519 + DFP + Fuel	0.25 meq/g
0.1 g	50	XE-519 + Fuel + DFP	0.21 meq/g
0.1 g	100	XE-519 + DFP + Fuel	0.23 meq/g

This page is intentionally blank.

C. PROTOTYPE MANUFACTURE (ACTIVITY C)

1. Summary

The primary objective of this contract was to develop prototype resin-based skin decontamination systems. Even the best sorbent/reactive resin system can be effective only if it is packaged in such a manner as to allow rapid and efficient delivery to the surface of the skin. The initial concept of using towelettes for delivery of wet systems and shaker cans for delivery of dry powders evolved into a unique delivery system that is felt to have significant advantages over conventional methods. The system which emerged consists of a flexible pouch, described in more detail below, containing the formulated decon resins. The lack of breakable components, such as glass ampoules, in the candidate system eliminate the need for a hard outer pack. Consequently, a soft pack pouch design was investigated and adopted as a preferable alternative to the final PCDS SDK prototypes.

2. Package Development

a. Delivery Systems

Shortly after the inception of work by Cosmetech, the search for a package development laboratory (PDL) was initiated. After numerous contacts, three companies were selected for final choice. Of these, Paco Pharmaceutical Services (PACO) of Lakewood, NJ, was considered to have the best capabilities to help develop a delivery system for the formulated decontamination resins under development. With the government's approval, PACO was selected.

Early concepts of delivery systems centered on shaker cans or rosin bags for dry powder formulations, and towelettes or tubes for cream and paste formulations. These concepts had undesirable features which made them unacceptable for its intended use.

What was desired was a method of delivery which was easy to use, was lightweight, could be deployed rapidly, and contained its own applicator. The development of the delivery systems of choice was evolutionary. What evolved was a flexible pouch delivery system, described below, useful for either powders or cream formulations.

Upon approval of the early concept of this design by the government (USAMMDA and U.S. Army Chemical School (USACMLS)), PACO prepared initial design drawings for the pouch and began fabrication of the semiautomatic filling and sealing equipment required for the preparation of the initial experimental prototypes and, later, the final PCDS SDK prototypes.

b. Decon Pouch Design

The new system utilizes an open weave resin-impregnated "carrier" pad adhered to a flexible backing. The carrier pad is a non-woven polyester fiberfill material. The open web nature of this material allows for a high loading of powder. The powder easily sifts out of the matrix when rubbed on the skin's surface. The fiberfill acts as a scrubbing surface to remove the agent-contaminated resin. The fiberfill is heat-sealed to the foil laminate. The entire pad is folded in half and sealed with a peelable heat seal on the edges to provide a single dose packet. A drawing of the pouch is shown in Figure 4. Figure 5 is a photograph of an opened initial prototype filled with powder.

The individual pouch concept has several advantages over other delivery systems. Each packet contains a single dose of resin. The matrix provides a certain amount of mechanical scrubbing action to aid in the physical removal of agent, including thickened agent. The resin is applied directly to the exposed skin.

The packet itself is made of a three layer foil laminate. The original plan was to use the same foil laminate that is used for the current M258A1 kit packet. The inner layer had to be changed for two reasons. First, the polyethylene inner layer of the M258A1 formed a permanent heat seal instead of the required peelable heat seal. Second, the polyethylene inner layer is a clear plastic which leaves the shiny foil exposed. The inner layer was necessarily changed to an olive drab vinyl coating.

The foil laminate used for the final PCDS SDK prototype consists of a 0.001-in. aluminum foil middle layer, a 0.0048-in. matte polyester film reverse gravure printed olive drab outer layer, and a olive drab vinyl heat seal coating inner layer. Each individual pouch (opened) is 2.75 in. in width by 11 in. in length containing a carrier pad of approximately 2 in. by 5 in. fiberfill on the foil laminate. When folded, it is designed to accommodate six pouches inside the current M258A1 hard outer pack, if desired. However, the PCDS SDK-designed outer container is a soft pack, described further in the next section.

The foil laminate is not sealed all the way to the ends, thereby leaving "flaps" for quickly peeling the pouch open. The pouches are packed in such a way that the "flaps" are upright in their outer holder for easy access even in MOPP gear. The individual pouches are designed with one flap up to be easily removed from the soft pack by a gloved hand. Each pouch contains a handle for grasping. Each pouch contains 2.8 g (±10%) of the decontaminant resin. Since the PCDS SDK is not classified as a drug by the FDA, each pouch has been labeled with the following minor warning located on the handle:

"CAUTION: MAY BE SLIGHTLY IRRITATING TO SKIN AND EYES"

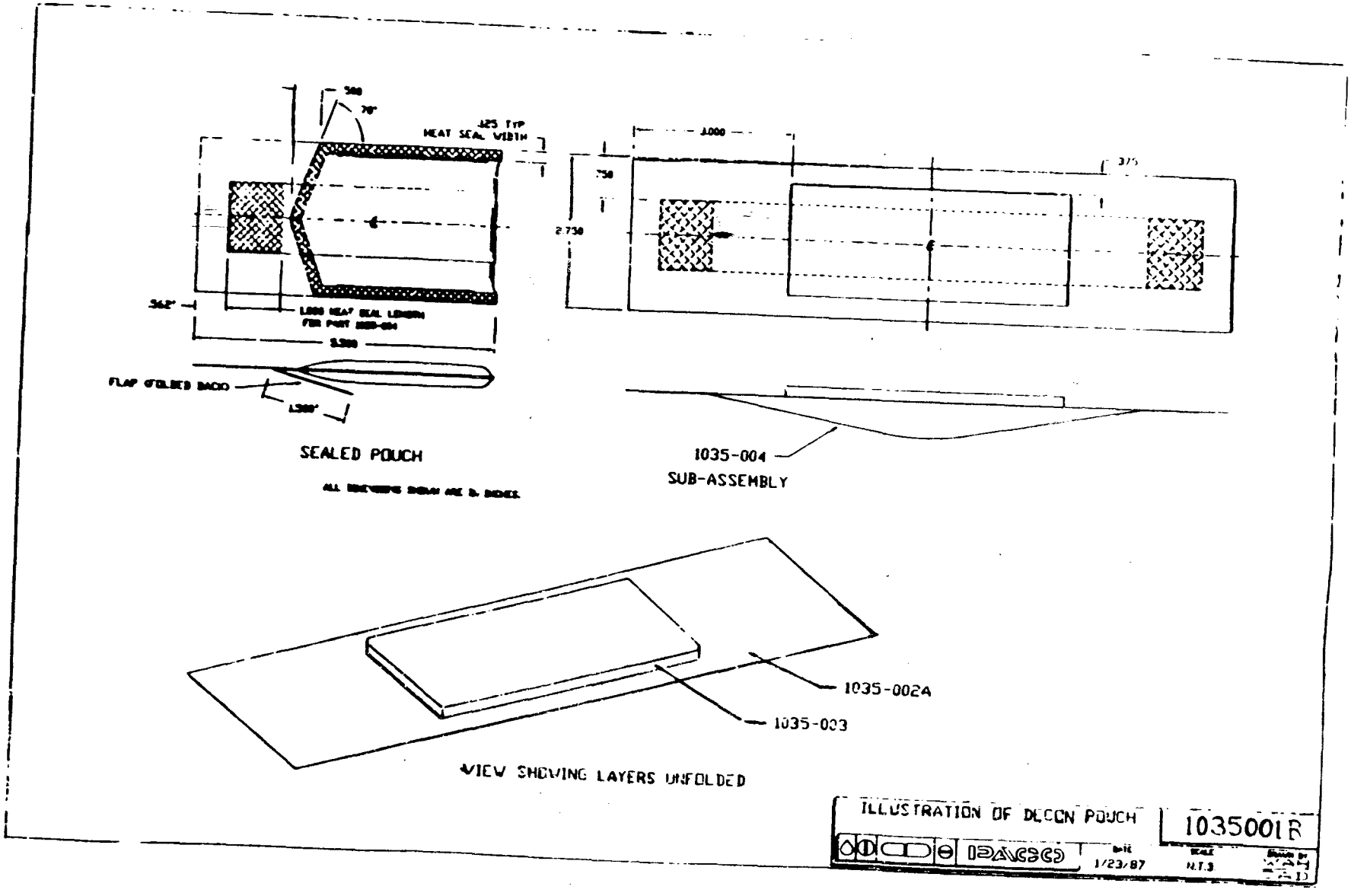


Figure 4

Illustration of Decon Pouch

(on facing page)

Figure 5

PCDS Skin Decon Kit
Opened Pouch - Powdered Formulation

PCDS SKIN DECON KIT

OPENED POUCH POWDERED FORMULATION

ROHM HAAS

In addition, simplified user instructions are printed on the flaps. A sketch illustrating the printing on the outside of the foil is shown in Figure 6.

c. Outer Soft-Pack Design for the PCDS SDK Prototypes

Discussions with USAMMDA and USACMLS led us to investigate various soft pack concepts to replace the hard M258A1 outer container. The concepts presented to the Army included accordion packs, tobacco pouches, surgical kits, zip lock pouches, change purses, bellows packs, and a partial wrap of the individual pouches (originally envisioned as a shrink wrap). The major trade-off of the various concepts was clearly the need for nuclear/biological/chemical (NBC) survivability of the outer soft pack versus a rapid and simple method of dispensing the individual pouches.

The "shrink wrap" concept was favored due to ease and speed of use. The NBC survivability was considered to be less important because of the protection afforded by the individual pouches (these would be NBC survivable) and the intermediate cartons (squad level) would eventually also be designed for NBC survivability.

It was decided that the soft pack must fit into the 7 in. by 8.5 in. flat Battle Dress Overgarment/Chemical Protective Overgarment (BDO/CPO) pocket. These are being phased out, but may still be in the system in 1990 when this kit is to be fielded. A larger pad can be incorporated as a Product Improvement Program (PIP) to use the larger Battle Dress Uniform/Overgarment 84 (BDU/OG84) pocket when the BDO/CPO is phased out.

Early prototypes of the outer soft pack were made from PVC. The material ultimately selected for use in the final prototypes was E.I. duPont's Tyvek polyolefin non-woven fabric, known for durability and toughness. This material can be also be printed upon. The design of the soft pack is shown in Figure 7 and in the photograph of the actual final PCDS SDK prototype (Figure 8). The soft pack is tinted olive drab and contains use instructions and a description of its contents. Three individual decon pouches are carried on each side of a perforated divider (hence, each PCDS SDK prototype holds six decon applications). The perforation is included for convenience so that the user can carry the SDK in more than one location, depending on doctrine.

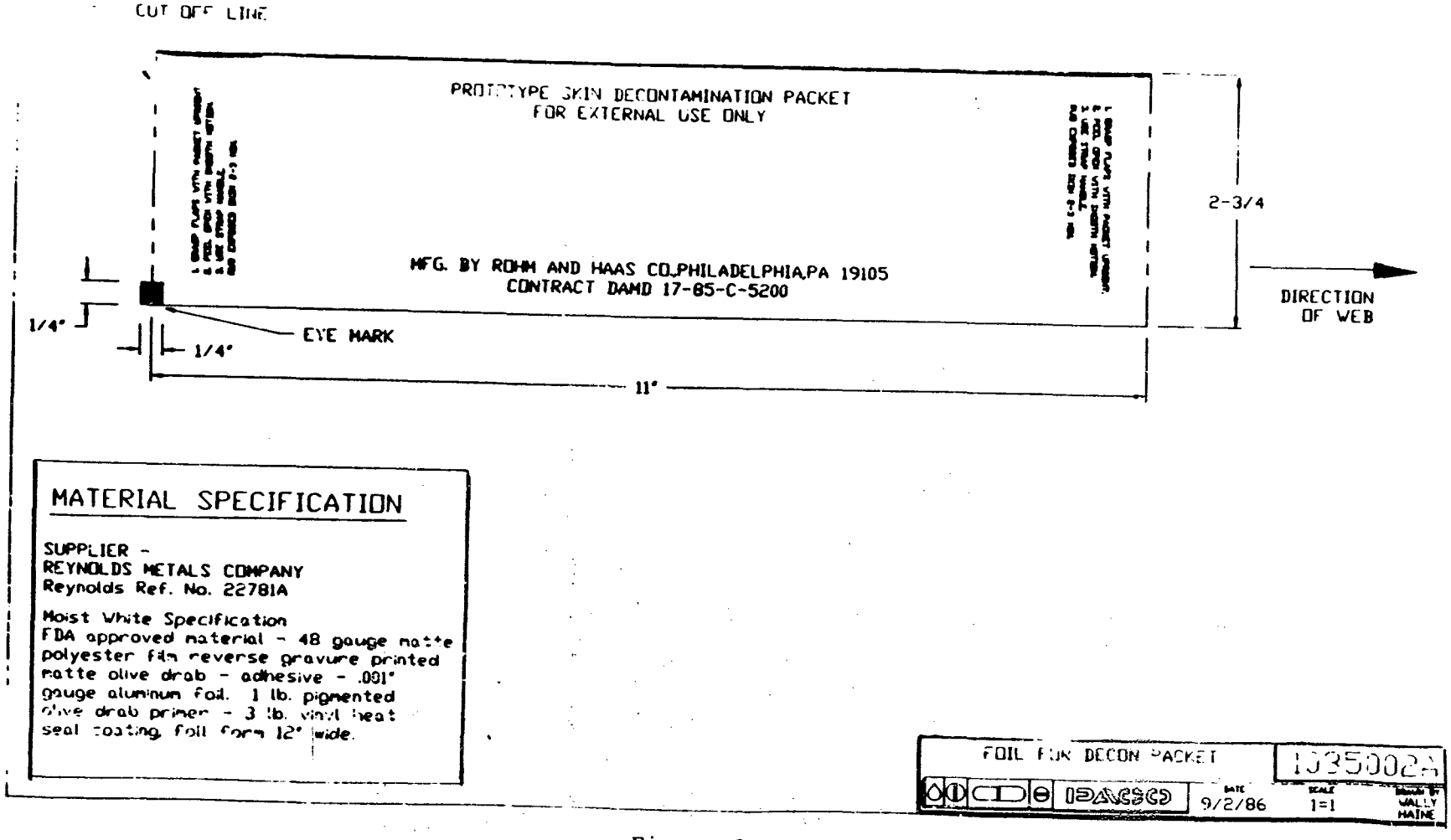
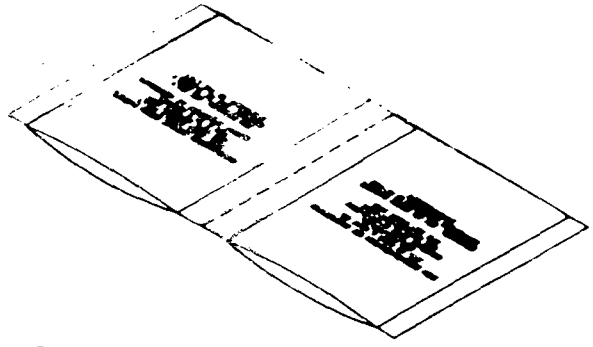
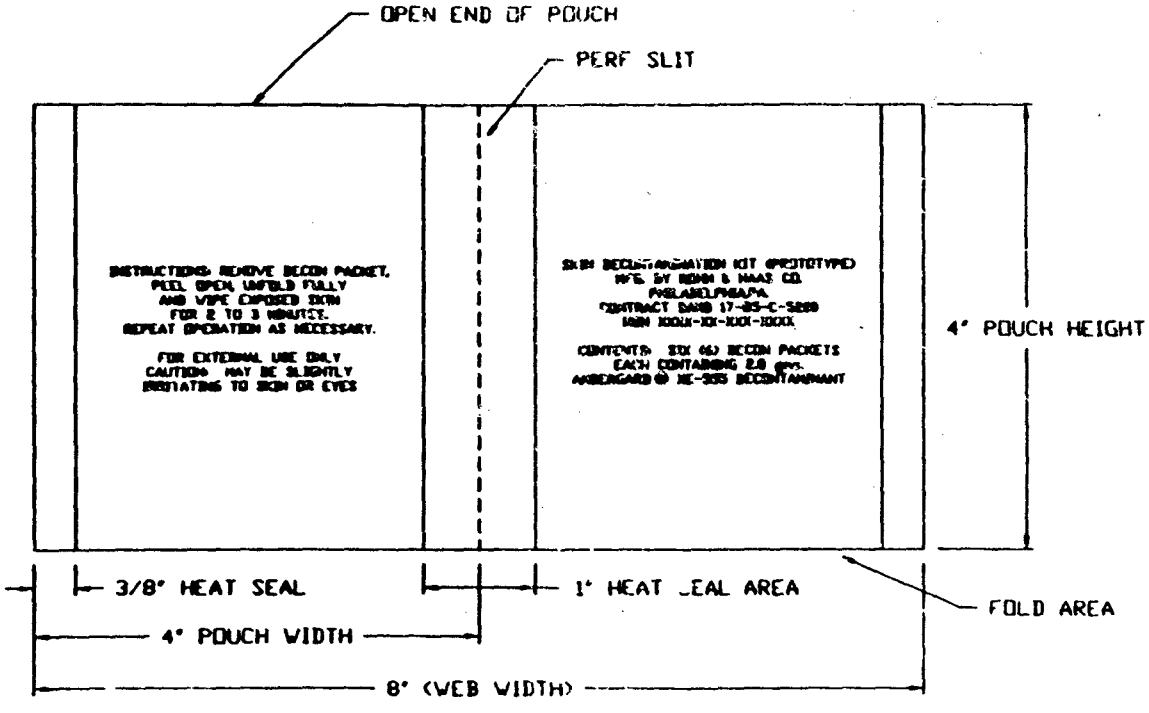


Figure 6

Foil for Decon Packet





REF. DWG. #1035008 FOR TYVEK WEB LAYOUT

ILLUSTRATION OF SOFT-PACK POUCH			1035009A
DAVCO	DATE 8/11/86	SCALE 1=1	DRAWN BY VALLY HAINE

Figure 7

Illustration of Soft-Pack Pouch

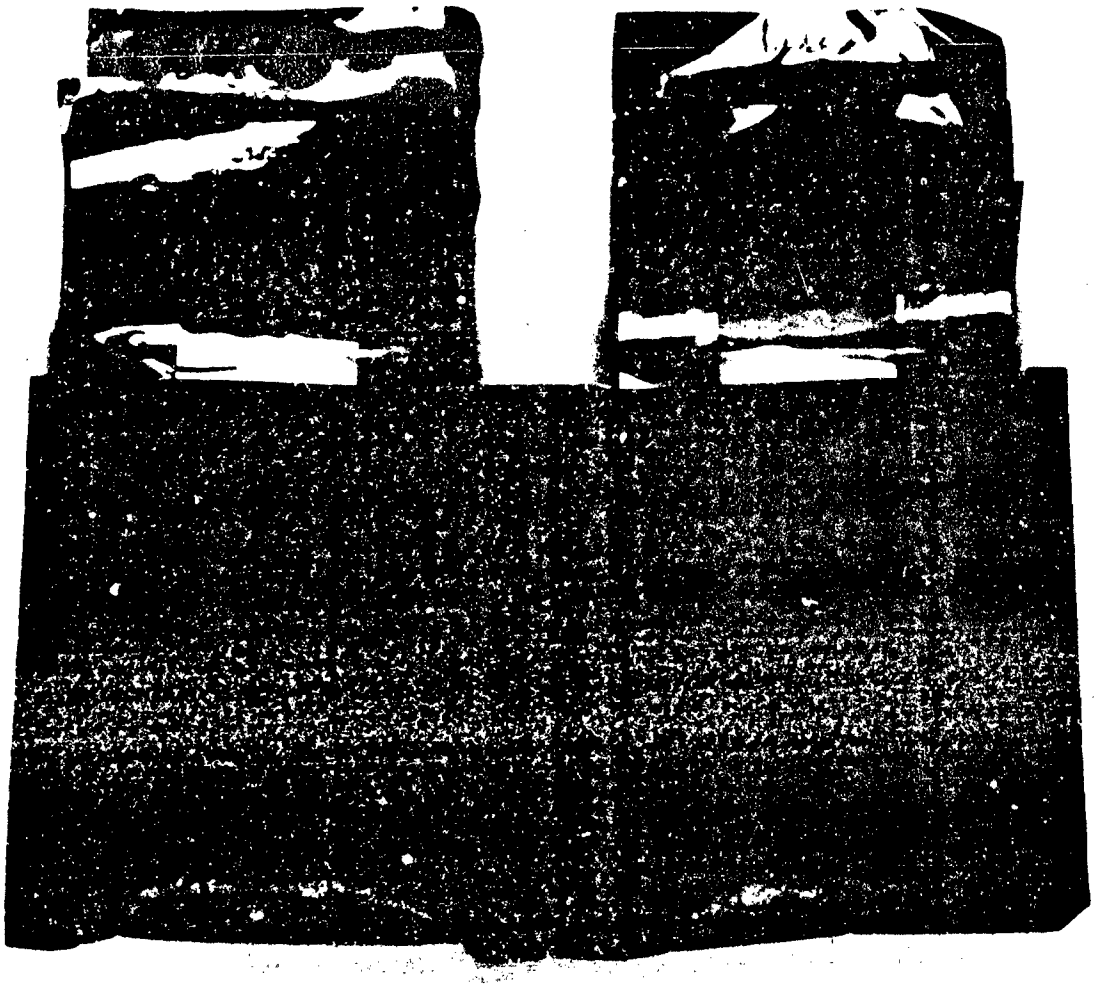
(on facing page)

Figure 8

PCDS Skin Decon Kit
Soft pack with Six Kits

PODS SKIN DECON KIT

Advanced Development Prototype



SOFT PACK WITH SIX PACKETS

ROHM AND HAAS

3. Prototype PCDS SDK Fabrication

It should be noted that, owing to the relatively small quantities of initial and final prototype kits required, and the time constraints of the project, the assembly of these kits was accomplished primarily by hand. However, special production tooling was designed and provided where necessary. The description below refers to the fabrication of the final prototype kits. With minor exceptions, it closely follows the procedure used in the production of the initial experimental prototypes assembled earlier in the program. The schematic diagram shown in Figure 9 describes the assembly process used by Paco Pharmaceutical Services to fabricate the final PCDS SDK prototypes under this contract. The process can be divided into three major stages: individual pouch (or packet) assembly, soft pack (or kit) assembly, and packoff (or shipping) assembly.

a. Individual Pouch Assembly:

The foil laminate is received in rolls from the supplier (Reynolds Metal Company), pre-printed with the desired legend and tinted olive drab on both sides of the foil (Reynolds Reference No. 22781A). The rolls are pre-slit to the specified packet width using the register marks printed on the foil. The foil is cut to length manually, also using the register marks as guides.

The fiberfill "carrier" pad is received from the supplier (Cumulus Fibres, Inc., Style 50W44) already cut to specifications (1-15/16 in. ± 1/16 in. wide, 5 in. ± 1/16 in. long, 1/2 in. thick). This nonwoven pad is heat-sealed to the unprinted side of the foil laminate. This assembly operation is performed in especially modified heat seal equipment designed to correctly position the carrier pad on the laminate foil and to provide the proper pressure/temperature/time (20 psi/325°F/1.7 s) profile for bonding the two together.

This heat-sealed sub-assembly is manually placed in the decon "doser" chamber, where either the powder Ambergard XE-555 or Ambergard XE-556 resin is loaded into the "carrier" pad. The bulk powder is held in a hopper, which is connected by tubing to the doser chamber. The hopper is vibrated continuously to prevent clumping and improve powder flow.

The carrier pad assembly is held by the retainer on the doser table. In a simultaneous actuation, this specially designed chamber is closed, a vacuum is applied to the carrier pad through the bottom of the chamber while nitrogen is applied to the top of the chamber, and a standard volume of powder (equivalent to 2.95 g (±10%)) is transferred into the carrier pad. The vacuum and nitrogen application is interrupted by a timing solenoid and the chamber opens. The operator removes the pouch, and at the same time, shakes off excess powder. The table is tilted to permit removal of excess decon powder. This step

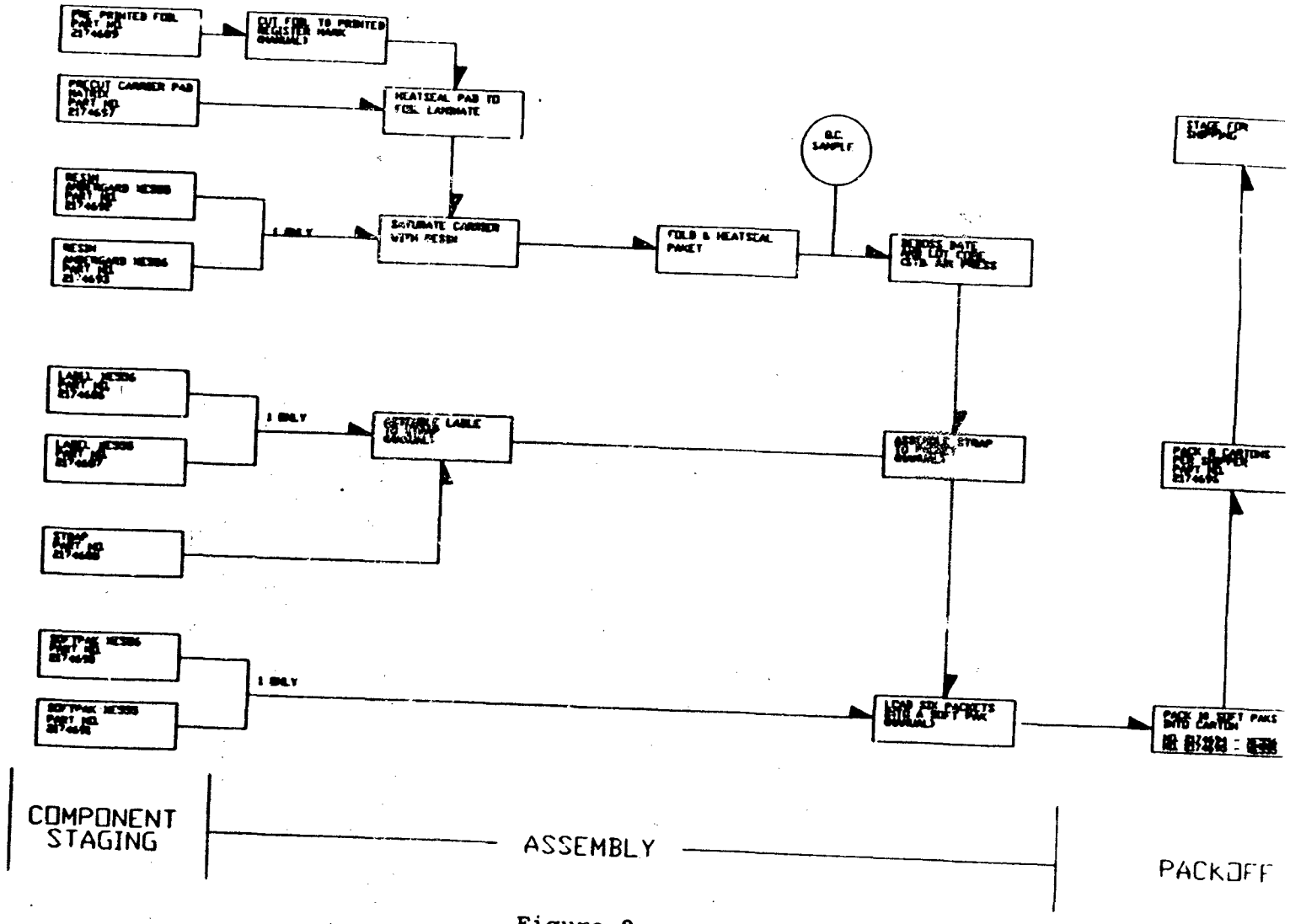


Figure 9

Block Diagram Decon Kit Assembly

consumes 1 to 2 s. This process step required complete redesign during final prototype fabrication as a result of formulation changes between the initial experimental prototypes and the final PCDS SDK prototype filling operation. The final powder-loading principle evolved after much redesign and experimentation. (For further details, see Prototype Production Summary section, below.)

This powder-saturated carrier pad is manually placed in a folder/sealer apparatus. This sub-assembly is placed in the proper position and the fold/seal cycle is initiated by the operator. The apparatus automatically folds each pouch and applies the proper temperature (375°F) and pressure (100 psi) to maintain a peelable heat seal. A heat-sealed pouch is sampled every 15 min for quality control purposes. The sample is weighed and tested for leakage by subjecting it to 20 in. Hg vacuum for 15 s.

The appropriate date/lot code is embossed on one of the tab ends of each pouch for additional identification and tracking. A specially designed polyester strap handle, supplied by Patton Company (Product # 60534XSCP), is manually attached lengthwise around the pouch after an identification label, designating the decon resin grade, net weight, and cautions for use, is attached to the strap handle.

b. Soft Pack Assembly:

The outer soft pack carrier consists of a pre-printed, olive drab, folded Tyvek spun-bonded olefin packet especially designed to hold six individual pouches, three in each of two compartments. The soft pack has a perforation between the two compartments, designed for convenient separation of the pack if so desired. This six-pouch assembly constitutes a single PCDS SDK prototype.

The soft pack and the designated legend are illustrated in Figure 7. The soft pack was designed by PACO, but fabricated by the supplier (Tolas Company) to specifications. Because each soft pack is pre-printed with the individual grade of decon material, the appropriate packet is selected depending on the grade of decontaminant powder being assembled. The six individual pouches are manually loaded inside the soft pack.

c. Packoff Assembly

It should be pointed out that this contract does not require production of the PCDS SDK prototypes beyond the soft pack assembly stage. This packoff assembly is provided for convenience in order to avoid damage of the prototypes during shipment. An attempt was made to satisfy the wishes of the user community by assembling the prototypes into cartons containing 10 PCDS SDK prototypes. (These cartons are also referred to as squad-size containers.)

Ten PCDS SDK prototypes are loaded vertically into each carton. This carton is supplied by PACO (either No. 2174694 or No. 2174695, depending on decon grade). The carton is pre-stamped with the appropriate grade of Ambergard resin decontaminant. The carton dimensions are 8 in. by 6.5 in. by 6 in.

Eight cartons (each containing 10 PCDS SDK prototypes) are loaded into each shipper box. This shipper box, supplied by PACO (No. 217496), is a corrugated cardboard box measuring 16-3/4 in. by 13-1/2 in. by 12-3/8 in.

4. Prototype Production Summary

The assembly of the final PCDS SDK prototypes was carried out initially in PACO's research building, as many aspects of the loading and filling operation had to be defined and corrected. Several approaches for loading the powder were investigated. During the fabrication of the initial experimental prototypes, the dosing of the decon powder was accomplished by drawing a measured volume of powder and depositing a compacted plug onto the carrier pad assembly. The powder was then forced into the pad manually as well as by vibrating the pad assembly. This approach was too time-consuming and did not work well, especially when the formulation was changed to Ambergard XE-555 and Ambergard XE-556 resins. The higher moisture content of the final formulations resulted in slowing the filling step further. Consequently, the loading and filling technique had to be modified as explained in the previous section.

Initial Ambergard XE-555 resin-filled prototypes were produced in the research building. After the filling procedure was streamlined, the entire process was transferred to PACO's production environment. At this point detailed production and quality control records were collected and the remaining quantities of final prototypes were fabricated. Table 19 summarizes the production history of the final PCDS prototypes.

Table 19

Production Summary of the PCDS SDK prototypes

Prototype Resin Grades	Lot No.	PCDS SDK Produced	Number of Cartons	Remarks
Ambergard XE-555	10/86 1	1000	100	Produced by research (old filling procedure)
Ambergard XE-555	10/86 1	140	14	Produced by production (old filling procedure)
Ambergard XE-555	11/86 1	1150	115	Produced by production (new filling procedure)
Total Ambergard XE-555 =		2290	229	Equal to 13,740 pouches
Ambergard XE-556	11/86 2	2290	229	Produced by production (new filling procedure)
Total Ambergard XE-556 =		2290	229	Equal to 13,740 pouches
TOTAL PCDS SDK PROTOTYPES =		4560	456	Equal to 27,480 pouches

5. Disposition of PCDS SDK Prototypes

The 4560 PCDS SDK prototypes produced in this contract were disseminated to the following groups:

Agency	Quantity (PCDS SDK)	Grade Ambergard Resin	Purpose
USACMLS	20	XE-555	Chemical School Instructor Familiarization/ training
USAMMDA	200	XE-555	User tests at Ft. Knox and Ft. Bragg.
USAMMDA	1800	XE-555	Completing contractual requirements
	2000	XE-556	

The remaining prototype kits were shipped to the Rohm and Haas Company Research Laboratories for use in various tests and evaluations.

6. Dusting Issues

This work was performed in response to the dusting issues raised during the customer testing conducted by the Engineer Test Division of the US Army Armor and Engineer Board (USAARENBD) at Ft. Knox and Ft. Bragg during November 1996. No attempt was made to fully resolve the issue in the limited time available. The purpose of this effort was to evaluate the feasibility of resolving the dusting issue within the time constraints of Request for Proposal (RFP) DAMD17-86-R-0146, "Full Scale Development and Initial Production of the Personnel/ Casualty Decontamination System Skin Decontamination Kit (PCDS SDK)." The fact that the working prototypes produced under the current contract would require additional design modifications was anticipated by the Army in the above mentioned RFP under Section C.6.1.1, Kit Design. These modifications would be incorporated into the 5,000 kits to be delivered 180 days after contract award (DAC).

Rohm and Haas Company's approach to this issue was, first, to evaluate the dusting question and, second, to consider potential approaches to address the issue during full-scale development (FSD). The approaches, in order of priority, were to include possible changes in (a) training and doctrine, (b) applicator design and (c) Ambergard XE-555 resin.

a. Investigation of the Dusting Issue

(1) Review of Customer Testing - The dusting issue was reported in the "Customer Test of The Personnel/Casualty Decontamination System, Skin Decontamination Kit (PCDS SDK)"; Final Report; CPT M.C. Silva, D.J. McCain (USAARENBD); January 1987. In addition to this report the individual comments of the test players were reviewed and a follow-up telephone conversation with CPT Silva was conducted. Information obtained from these sources is summarized below.

During the Ft. Knox phase of testing, the six players were not permitted to actually apply the kit to their skin, since a safety release had not been provided in time. During the Ft. Bragg phase of testing, players were required to decontaminate their faces while wearing the protective mask. While the soldiers were conducting facial decontamination, six of the soldiers experienced some coughing and complained of difficulty breathing for about 5 to 10 s.

In follow-up conversations, it was discovered that this was the first and only time these soldiers had applied the resin powder to the face. That is, it appears that they had limited opportunity to familiarize themselves with the PCDS SDK. Furthermore, the soldiers used fresh packets on their faces. While some confusion exists as to the optimum use protocol, the protocol in the Training Test Support Package (TTSP) PCDS SDK instructs the soldier to decontaminate the hands prior to decontamination of the face, using the same packet. Decontaminating the hands first may reduce the amount of free powder during the subsequent facial decontamination. These observations are not intended to be criticisms of the user tests, but merely to identify possible contributory factors to this dusting problem, and point out the importance of developing more precise use instructions for the PCDS SDK during full scale development. In any event, the dusting issue is real and merits further investigation. This is addressed further below.

(2) Decontamination under the M17A2 Mask - In order to appreciate fully the dusting issue, four Rohm and Haas personnel conducted various facial decontamination procedures under the M17A2 mask. Two use protocols were investigated. First, in an attempt to replicate the customer testing, the decontamination was conducted on the face with a fresh packet. During this first protocol, after clearing the mask, the subjects initially breathed through their mouths. In the second protocol, the facial decontamination was conducted after decontamination of the hands, using the same pad. In this case, after clearing the mask, the subjects initially breathed through their noses. During some of these facial decontamination trials, the breathing space was sampled, using an air sampling assembly to quantify the amount of dust present.

Using the first protocol (full packet on face), three of the four subjects reacted by coughing. In all cases, these coughs were slight and in the subjects' opinions, not significant, i.e. were not at all incapacitating. The coughing response was not noted when using the second protocol, however. The dust collected using the air sampling device is summarized in Table 20. Since the measurable quantity is near the detection limit of the technique, a visual observation of the black powder on the collection membrane is also noted.

Table 20

Summary of Rohm and Haas Testing of
Facial Decon Under the M17A2 Mask

Subject No.	Protocol No.[a]	Filter Weight Gain, g	Coughing Noted	Collected Dust, visible
1	1	0.00006	yes	yes
1	1	0.00003	yes	yes
2	1	0.00025	no	yes
2	1	[b]	yes	
2	2	0.00002	no	slight
3	1	0.00009	no	yes
	[c]	0.00008	no	no
3	2	0.00002	no	yes
4	1	[b]	yes	
1	control[d]	0.000035 ± 0.00012		no

[a] See text for protocol.
[b] No air sampling during this run.
[c] Fresh filter used after 10 min, no additional dust noted.
[d] Average of four membrane weight changes with no resin ±2 standard deviations.

Indeed, in experiments performed under laboratory-controlled conditions, some coughing was observed. However, this limited study also suggests that changes in use protocol i.e. application instructions) can significantly mitigate the coughing tendency.

b. Possible Solutions

(1) Alternate Kit Designs - The advanced development prototypes used in the customer tests were not optimized. The requirement for design modification as a result of the user testing was anticipated by USAMMDA in RFP DAMD17-86-R-0146. While the kit design will be addressed in detail in the subsequent contract, the feasibility of reducing the dusting through design modifications was demonstrated. Several hand-made samples were made and demonstrated in a videotape especially prepared by Rohm and Haas for the In Process Review (IPR) I/II,

entitled "Approaches to Prototype Kit Dusting Question." This video was provided to USAMMDA and was shown at the IPR.

Three approaches were taken to reduce the amount of free powder upon opening the individual pouch. First, the powder was loaded under the nonwoven fiberfill matrix. Second, various densities of fiberfills were investigated, which were shown to control the rate of powder delivery. And finally, a scrim covering the resin-loaded fiberfill was investigated. All of these approaches limited the amount of free powder, as was clearly demonstrated in the videotape. These approaches do not exhaust the possible design modifications. They do indicate that the amount of free powder can be controlled through minor kit modifications.

(2) Change in Resin Particle Size - Respirable dust is directly relatable to particle size. While this has not been investigated, we have sufficient control over our resin grinding procedures to produce Ambergard XE-555 resin with a larger mean particle size. (Some particle size data as a function of grinding time are presented in Section F below.)

Particle size measurements are typically run on liquid suspensions of the powdered resin. It is possible that aerosol particle sizes may differ from the liquid suspension particle size owing to aggregation as a result of charge or moisture content. As a result, an attempt was made in the limited time available to try to quantify the effect of grinding conditions on the amount of aerosol particles from a given sample.

Several samples of the Ambergard XE-555 resin prepared at different grinding times (Section F) were evaluated by Rohm and Haas Company's Inhalation Toxicology Group for aerosol particle size. The test involved dispersing small quantities of each sample into the incoming airstream of a cylindrical air chamber and collecting aerosol particle size data. Unfortunately, this test protocol was designed for a different application and, consequently, the test results obtained were not conclusive. While it was demonstrated that all samples contained respirable dust, the sampling of the air chamber excluded all but the fine material. It was not possible to ascertain what portion of the total resin was actually sampled. As a result of these sampling difficulties, different grindings of resin and different moisture contents all appeared the same.

(3) Change in Resin Formulation - Formulation excipients were purposely kept to a minimum in order to provide the maximum concentration of active resins in the Ambergard XE-555 resin. Further reformulation to reduce dusting would be possible, but is not desirable if not absolutely necessary. The current systems have been extensively characterized in in vitro and in vivo efficacy testing and toxicological studies. Slight formulation changes may not significantly alter these properties, but the effects of extensive changes would not be known.

c. Conclusions/Recommendations

The results of this limited study indicate that the dusting question noted during the customer tests are readily resolvable.

While the follow-on contract allows for a more extensive evaluation of design modifications, based on the available information, Rohm and Haas can make some preliminary recommendations. Our position as to the best course of action may change as more information is available, and no firm decision should be made at this time.

We recommend that although some kit modifications will be necessary, the dusting issue be addressed primarily through training and doctrine. As reported above, we did not note any coughing when the kit was properly applied after first decontaminating the hands. In the event that only the face needs decontamination, the free powder could be removed by momentarily turning the packet over if the coughing noted was considered significant. This recommendation is made in view of the trade-off involved. We can easily reduce the amount of resin in the packet or reduce the rate of delivery through design modifications. However, it is this available resin that decontaminates the chemical agent on the skin surface. A decrease in the available resins will result in a corresponding decrease in the decontamination capacity. We may need to reduce the amount of free powder, but not to the extent to reduce the SDK efficacy or capacity.

7. Additional Packaging Concepts

a. Chemical Hardening in Accordance with AR 70-71

Current Army regulations (AR 70-71) "Nuclear, Biological, and Chemical Contamination Survivability of Army Material" (May 1984) will require that the squad containers for the SDK be impervious to chemical agents and be decontaminable. An effort was begun to investigate concepts for meeting this requirement. The Army has stated that they do not want a heavy, rigid "ammo box"-type squad container. The current concept is to use a lightweight cardboard box with some type of protective coating or over-wrap.

(1) Chemical Agent Resistant Coatings - Level A military packaging requirements for some applications requiring cardboard boxes specify that all seams be sealed with duct tape and a fiber reinforcing tape. Samples of cardboard taped with both duct tape and fiber reinforcing tape were obtained from a packaging company experienced in military packaging. These samples were sent to Mobay Chemical Corp., Pittsburgh, PA, to be coated with several different sealer systems and a chemical-agent-resistant coating (CARC). These CARCs were developed for protection of military

equipment (MIL-C-46168C(ME), "Coating, Aliphatic Polyurethane, Chemical Agent Resistant," 28 March 1984).

Primers (sealers) of various flexibilities were evaluated. All samples were top-coated with approximately 2 mils or 4 mils of CARC. Mobay reported all samples passed the DS-2 test of MIL-C-46168C. Mobay reported good adhesion to the cardboard, but no system tested adhered to the duct tape. We found the fibers in the cardboard to be protruding through the CARC in some cases, which might be expected to wick agent into the cardboard. Also the coating tended to chip if the samples were flexed.

Mobay has agreed to coat several more samples with a low- or non-pigmented CARC. The samples described above were olive drab. The pigmentation decreases both the chemical resistance and the flexibility of the CARC. The pigmentation is required to meet UV reflectance specifications for many military applications, but will likely not be required for our application.

(2) Protective Over-Wrap - An alternative to the coating approach would be to seal the box in a plastic wrap. Several chemical companies were contacted to obtain information on barrier films. Dow Chemical Co. manufactures a polyvinylidine protective film, Saranex, which has been used as a barrier against chemical agents. This material is heat-sealable and can be handled in commercially available packaging equipment. Samples of a Saranex backed with E.I. du Pont's Tyvek spun-bonded polyolefin, used for protective garments, were obtained from Dura-Fab, Inc. (Rowley, MA). Samples of Saranex film and bags were obtained from Dow. No testing has been done on the samples.

In our investigations of sources for barrier films, we learned that Geomet Co. was performing live agent testing on Saranex under Air Force contract F33657-82-C-0435. We have requested that our COR, LTC Harrington, contact the appropriate Air Force representative to obtain permission for Rohm and Haas to have access to the data that might apply to our application.

b. Alternate Applicator Pad Materials

The nonwoven fiberfill used in the advanced development prototype was not optimized, as the object of the current contract was to demonstrate feasibility of various applicators. While we will not be able to incorporate any changes into the current prototype, the issue is being investigated for future development.

Six samples of different nonwovens were obtained from Kem-Wove Inc., Charlotte, NC. A brief description of each sample is shown in Table 21. The fiberfill used in the prototype kits was from a different supplier, but is similar to the CBC 4.0. The SCN 86-2 and SCN 86-8 are characterized by a much finer denier (fiber thickness), resulting in a denser material.

Table 21

Description of Nonwoven Fiberfill Materials

Sample	oz/yd^2	Firmness	Denier
CBC 3.0	3.0	"Soft Hand"	4.75-6
CBC 3.0UB	3.0	Firmer	4.75-6
CBC 4.0	4.0	"Soft Hand"	4.75-6
CBC 1.85	1.85	"Soft Hand"	4.75-6
SCN 86-2	4.0(est)	"Soft Hand"	1.5
SCN 86-8	4.0(est)	"Soft Hand"	blend

The powder flow through the different nonwovens was evaluated by placing 1.0 g of Ambergard XE-555 resin in the top of an 8-oz. jar lid, covering the lid with the nonwoven, and screwing the jar onto the lid. The jars were turned upright and placed, six at a time, onto a shaker for 1.0 min. The powder sifting through the fiberfill was weighed and the average of triplicate runs are reported in Table 22. These results demonstrate that the rate of resin delivery may be controlled by proper selection of the matrix. The results for the small denier material indicate that this construction may be too dense for our purpose.

Table 22

Results of Fiberfill Shake Test

Smmple	Weight of Resin through Pad, g	Standard Deviation
CBC 3.0	0.139	0.021
CBC 3.0UB	0.111	0.022
CBC 4.0	0.135	0.111
CBC 1.85	0.289	0.122
SCN 86-2	0.011	0.012
SCN 86-8	0.016	0.005

Some hand-made sample packets were made in the laboratory with selected fiberfill matrices. These are discussed above under the dusting issue section.

D. TOXICOLOGY (ACTIVITY A)

1. Toxicology Results on the Unformulated Decon Resins

a. Dermal Penetration Studies on XE-522 Containing Radionuclide-Labeled Anionic Component

In vitro and in vivo dermal penetration studies were completed on XE-522 containing ^{14}C-labeled anionic component.

IN VITRO:

A Rohm and Haas Company strong base ion exchange resin Amberlite (^{14}C-IRA-900) resin was blended with non-radiolabeled Amberlyst XN-1010(H) resin and Ambersorb XE-348F adsorbent (Rohm and Haas reactive- and sorbent-type resins, respectively) to yield the experimental skin decontaminant resin XE-522. This material was applied as a 14% aqueous suspension to freshly excised female rat skin mounted in Franz Diffusion Cells. The ^{14}C-resin blend remained on the skin for 5.0 min, or 2.0, 6.0, 24, or 48 h prior to removal by washing with cotton swabs moistened with water. Following removal of the ^{14}C-resin blend, ^{14}C-label was accounted for by analysis (liquid scintillation counting, LSC) of: a) the atmosphere in the chamber above the skin, b) the wash material, c) the skin, d) the Tyrode's bathing solution beneath the skin, and e) the lower cell wash.

Results: Only 0.08% to 0.21% of the applied ^{14}C-label penetrated through the skin. Penetration occurred rapidly (5 min), but did not increase with prolonged exposure time (48 h). An additional 0.11% to 0.67% of the applied ^{14}C-label was found in or on the skin after washing. The amount of ^{14}C-label in or on the skin decreased as exposure time increased. This decrease was apparently due to drying of the aqueous resin, which subsequently resulted in more efficient removal during the wash-off procedure. Thus the ^{14}C-label found in the skin is residual ^{14}C-label not removed in washing. Total absorption including ^{14}C-label found in the skin was 0.27% to 0.86% of the applied ^{14}C-label during the exposure period of 5 min to 48 h.

Conclusion: Very small quantities (0.08% to 0.21% of the applied ^{14}C-label) penetrated rat skin in the in vitro system. Penetration was rapid (within 5 min) and did not increase with prolonged exposure time (up to 48 h).

IN VIVO:

A Rohm and Haas Company strong-base ion-exchange resin (^{14}C-IRA-900) was mixed in a typical aqueous blend with other reactive- and sorbent-type resins to yield the experimental skin decontaminant XE-522. This material was applied to the backs of female Sprague-Dawley rats (300 microliters or 42 mg per 10

square centimeters of skin) for various exposure times up to 96 h.

Results: Small amounts of ^{14}C-label were detected in whole blood, liver, and kidneys within 1 to 2 h after dosing. Excretion of ^{14}C-label in urine and primarily feces occurred within 6 to 24 h after dose application. Fecal ^{14}C-label excretion accounted for a mean of 4.0% of the applied dose at 24 h after dosing. Whole-blood ^{14}C-label concentrations were highest at 2 h after dosing (4 ppm) and ^{14}C-label was still present at 96 h after dosing. No ^{14}C-label was found in plasma 48 h after dosing, but it was present 96 h after dose application. Liver ^{14}C-label concentrations were highest 2 h after dosing (0.12 ppm) and decreased to non-detectable levels by 96 h after dose application. Kidney ^{14}C-label concentrations were also highest at 2 h after dosing (0.23 ppm) but decreased to non-detectable levels by 6 h after dose application (except for one of four animals at 96 h after dosing). Some ^{14}C-label (5.0% to 6.5%) remained in or on the skin after washing at 1, 2, or 6 h after application. At 24 h after dosing, the ^{14}C-label found in the skin had decreased considerably. An increase in fecal ^{14}C-label excretion was also observed at 24 h after dosing. No corresponding increase in tissue ^{14}C-label concentration was observed. Residual ^{14}C-label left in or on the skin may penetrate the skin with time and subsequently be excreted in the feces.

Concludions: Based on excretion data, application of the ^{14}C-labeled resin (XE-522) to the backs of rats for 6 h resulted in the absorption of approximately 4% to 6% of the applied ^{14}C-label. Most of the absorbed ^{14}C-label was rapidly excreted in urine and primarily in the feces within 6 to 24 h after dose application.

b. Acute Inhalation (rats) of XE-519, XE-521, XE-523, XE-525 and Fuller's Earth (control)

Male and female Sprague-Dawley rats received single whole-body 4-h exposures to a dust aerosol of each of the above resin systems or fuller's earth at an analytical concentration of 4.5 to 5.3 mg/L and an aerosol particle size distribution with a mass median diameter of 5.4 to 8.4 micrometers, a geometric standard deviation of 1.8 to 3.2, and respirable fractions of 16% to 52%. The animals were held for 14 days after exposure, during which period clinical signs and body weights were monitored. Necropsies were performed on all animals at the end of the 14-day observation period.

Results and Conclusions:

XE-519 - The results indicate that this resin blend was a sensory and upper airway irritant, and a central nervous system depressant resulting in reduced body weight and body weight gain. Treatment-related necropsy observations were typical of a

response by the respiratory system to the inhalation of an insoluble particulate at concentrations in excess of the normal clearance capacity of the lungs. The estimated LC_{50} for male and female rats was greater than 5.1 mg/L.

XE-521 - Results indicate that this resin blend was a sensory and upper airway irritant and resulted in reduced body weight and body weight gain. Two male rats died on the day of exposure due to hypoxia, caused by physical blockage of the trachea by the test substance. Treatment-related necropsy observations were typical of a response by the respiratory system to the inhalation of an insoluble particulate at concentrations in excess of the normal clearance capacity of the lungs, and secondary effects of hypoxia. The combined male and female LC_{50} was greater than 5.1 mg/L of air.

XE-523 - All animals died during the exposure owing to hypoxia produced by physical blockage of the trachea by the resin. This study was to have been repeated, but XE-523 was deemed to be of no further commercial interest. Therefore, all data on this resin were placed in the Toxicology Department Archives and further work was canceled.

XE-525 - Results indicate that this resin was a sensory and upper airway irritant and resulted in reduced body weight and body weight gain. Treatment-related necropsy observations were typical of a response by the respiratory system to the inhalation of an insoluble particulate at concentrations in excess of the normal clearance capacity of the lungs. The combined male and female LC_{50} was greater than 5.3 mg/L of air.

Fuller's earth - Results indicate that fuller's earth was a slight sensory and upper airway irritant and resulted in transient reduced body weight and body weight gain. Necropsy of all animals at the end of the observation period revealed no treatment-related lesions. The combined male and female rat LC_{50} was greater than 4.5 mg/L of air.

c. Sub-acute Inhalation (rats) on Ambergard XE-519:

Male and female rats received whole-body inhalation exposure for 6 h per day for 10 days over a two-week period to air, fuller's earth dust, or Resin XE-519. Half of the animals in each group were necropsied immediately after the two-week exposure period, and the remaining animals were necropsied after a four-week recovery period.

Results and Conclusion: Using the presence of inflammation in the respiratory tract as the minimum criterion for an adverse effect, the lowest-observed-adverse-effect level (LOAEL) for Resin XE-519 was 320 mg/m^3, based on total concentration, and 117 mg/m^3, based on respirable concentration. The no-observed-adverse-effect level (NOAEL) was 12 mg/m^3, based on total concentration and 7 mg/m^3 based on respirable

concentration. After four weeks of post-exposure recovery, the NOAEL was unchanged.

Results also indicated that rats exhibited a greater toxic response after inhalation exposure to fuller's earth at a total concentration of 1174 mg/m^3 (359 mg/m^3, respirable) than to a comparable total concentration of Resin XE-519 of 1094 mg/m^3 (428 mg/m_3, respirable)

d. Human Irritation/Sensitization Studies on the Unformulated Resins

Human irritation/sensitization studies to investigate the skin sensitization potential of the unformulated resins XE-520, XE-522, XE-524, and XE-526 were conducted at Hill Top Research Laboratories, Inc., St. Petersburg, FL.

Fifty-six to 57 male subjects began the testing with each resin system and 48 to 51 subjects completed all phases of the experimental plan in each case. Applications of the aqueous resin were by 24-h contact occlusive patches to the same skin site three times per week for three weeks (induction period), followed by a rest period in which the subjects did not receive any application of the resin for approximately two weeks. Following the rest period, a "challenge" application was made to a naive skin site to test for reactions indicative of contact sensitization. Simultaneous application to a "pre-exposed" site (original induction site) was made concurrently with the challenge application.

Results:

XE-520 - None of the 50 subjects completing the test exhibited a response during the challenge period. No skin irritation was observed during any phase of the study.

XE-522 - None of the 48 subjects completing the test exhibited a response during the challenge period. Only an occasional occurrence of irritation was observed during the induction period.

XE-524 - One of the 50 subjects completing the test exhibited a response during the challenge period. This response was mild however and indicative of primary irritation.

XE-526 - One of the 51 subjects completing the test exhibited a response during the challenge period. This response was mild however and indicative of primary irritation. Only an occasional occurrence of irritation was observed during the induction period.

Conclusion: Based on the above results, it was concluded that none of the resin systems tested showed any evidence indicative of delayed contact sensitization.

2. Toxicology Results on the Formulated Decon Resins

a. Thirteen-Week Dermal Toxicity/One Generation Reproduction Study in Rats

XE-551 was tested in a 13-week dermal toxicity/one generation reproductive study in rats. A 25% (wt/vol) aqueous dispersion of XE-551 (corresponding to a dose of 500 mg/kg or 31.3 mg/cm^2) was applied unocclusively (2.0 mL/kg) to the intact skin of rats. Male rats were dosed once daily for 11 weeks prior to mating (5 days per week) and during a two-week mating period (7 days per week). Female rats were dosed once daily for two weeks prior to mating (5 days per week) and daily (7 days per week) during the mating period and from days 0 through 16 of gestation. Dams were allowed to deliver naturally. After a four day lactation period, dams and pups were sacrificed. A control group of rats was dosed in the same manner with distilled water.

All animals were monitored daily for signs of ill health or reaction to treatment, and skin irritation was evaluated twice weekly. After 13 weeks of treatment (i.e., after the mating period), all male rats were bled for hematology and clinical chemistry evaluation, sacrificed, and necropsied, and the liver, kidneys, adrenals, and testes were weighed. Male and female reproductive parameters, pup survival, and pup body weights were evaluated during the reproductive phase of the study.

Results: No treatment-related deaths occurred and no clinical signs indicative of systemic toxicity were observed in any of the treated or control animals. Minimal skin irritation (i.e. grade 1 erythema) was seen in males on days 4 and 7 of the study. No other skin irritation was seen during the study. No significant differences between control-and treated-animal populations were noted in mean body weight and body-weight change during the pre-mating, gestation, or lactation periods. Treatment of males with XE-551 had no toxicologically significant effects on any of the hematology or clinical chemistry parameters evaluated or organ weights measured.

No adverse effects were detected for any adult male or female reproductive parameters. The mean number of pups per litter and the total number of pups delivered were greater in the treated group compared to the control group. No stillborn pups were found in either group. Six pups in four litters in the treated group died post-partum (PP) (day 0), while none died in the control group. Survival to day 4 PP was slightly decreased in the XE-551 treated litters when compared to control litters (93% vs. 98%). These changes were not considered treatment-related, since one-half of all the deaths in the treated group occurred in unusually large litters (18 or more pups). Four of the 14 dams in the treated group had litters with 18 or more pups (in three of these litters deaths occurred), while no control litters exceeded 17 pups. Mean litter weight on day 0 PP was

similar between the control and treated groups. Decreased mean litter weight on Day 4 PP was noted in the treated group when compared to the control group. This decrease was not considered treatment-related, since slight decreases in mean litter weight are common in unusually large litters.

Conclusions: No treatment-related signs of toxicity were observed in male rats following 13 weeks of dermal treatment (500 mg/kg) with XE-551. No adverse effects were detected for any adult reproductive parameters after exposure to XE-551. No treatment-related effects were noted on pup survival or pup body weights.

b. Acute Toxicity of Ambergard XE-555 and Ambergard XE-556 Resins

Acute Toxicity Profile Testing (oral LD_{50}-rats, dermal LD_{50}-rabbits, skin and eye irritation) was completed with Ambergard XE-555 and Ambergard XE-556 resins.

Results: Both resins are practically non-toxic by ingestion of a single dose (male rat LD_{50} is greater than 5.0 g/kg).

Both resins are practically non-toxic by a single dermal application (male rabbit dermal LD_{50} is greater than 5.0 g/kg).

Both resins are practically non-irritating to the skin of rabbits (72-h mean irritation score (MIS) is 0).

Both resins are inconsequentially irritating to the eyes of rabbits (no ocular effects were observed at 24 h or within 7 days).

c. Human Irritation/Sensitization Studies on Ambergard XE-555 and Ambergard XE-556 Resins

Human irritation/sensitization studies to investigate the skin sensitization potential of the final two formulated resin systems, Ambergard XE-555 and Ambergard XE-556 resins, in males and females, were also completed at Hill Top Research Laboratories, Inc. The following summarizes this investigation.

Male and female subjects, 60 in all, began the testing with Ambergard XE-555 and Ambergard XE-556 resins and 54 to 55 subjects completed all phases of the experimental plan in each case. Applications of an aqueous dispersion of each resin were by 14-hour contact occlusive patches to the same skin site three times per week for three weeks (induction period) followed by a rest period during which the subjects did not receive any application of the resin for approximately two weeks. Following the rest period, a "challenge" application was made to a naive skin site to test for reactions indicative of contact sensitization. Simultaneous application to a "pre-exposed" site

(original induction site) was made concurrently with the challenge application.

Results:

XE-555 - None of the 54 subjects completing the repeated insult patch test exhibited a response to XE-555 during the challenge period. No skin irritation was observed during any phase of the study.

XE-556 - Of the 55 subjects completing the repeated insult patch test, one subject exhibited a response to XE-556 during the challenge period. This response was classified as mild erythema indicative of irritation and subsided by the 96-hour scoring.

Conclusions: Based on the above results, it was concluded that neither XE-555 or XE-556 showed any evidence of delayed contact sensitization or significant skin irritation.

This page is intentionally blank.

E. IN VITRO CHEMICAL AGENT TESTING (ACTIVITY B)

This section pertains to the chemical surety testing performed by Midwest Research Institute (MRI). It is divided into four sections:

1. Rohm and Haas's introduction and comments regarding the agent work;
2. The final report submitted by MRI;
3. Comparison of the agent data to simulant data obtained at Rohm and Haas.
4. Vapor desorption properties and reactivity of stressed resin samples.

1. Introduction

Chemical surety testing of candidate resin systems was conducted by Midwest Research Institute under subcontract to Rohm and Haas. MRI's Final Report is included following this introduction.

The testing described in the MRI's report involves four resin systems: XE-519, XE-521, Ambergard XE-555, and Ambergard XE-556. The objectives of this testing were to determine if the formulated Ambergard resins were any less efficacious than the unformulated resins, to determine whether either of the formulated Ambergard resins demonstrated a significant advantage over the other; and to obtain an estimate of the efficacy of the resins at realistic resin to agent concentrations based on the in vitro tests.

MRI used the same five in vitro test methods that were developed by Rohm and Haas for their agent evaluation of resin systems. Some minor protocol modifications were necessary to meet surety safety and handling requirements. These protocol development issues were reported in detail in the 1986 Annual Report[1]. The same caveat mentioned for simulant test must be repeated here. The tests were designed to rank resin systems, not to yield 'real world' results. For example, our Liquid Sorption Test ranks the wettability of powdered systems, but does not take into consideration any mechanical mixing due to rubbing. It is important to consider the results within the context of the test conditions and not to over-interpret the data.

The agent dose "use level" referred to in MRI's report is defined as 15% of the resin weight (15 µL agent/100 mg resin or 15 mg agent/100 mg resin). This is based on an area coverage target of 1300 cm^2, a challenge threat of 2.5 g/m^2, and 2.8 g of resin per kit. (The actual JSOR requirements specify three decontaminations of 1300 cm^2 each. As the final kit has six packets, a value of 650 cm^2 for area coverage could be used. The use level defined above is twice as stringent as the requirements.)

2. Midwest Research Institute Final Report

Following is the Final Report submitted by MRI for the chemical surety testing of the candidate resin system under this contract. The table and figure numbers of MRI's original report have been changed for the sake of clarity and continuity. Comments and additions made by Rohm and Haas are indicated in the text by brackets, [ ].

a. Introduction

Midwest Research Institute (MRI) performed the chemical surety testing of Rohm and Haas resins on USAMRDC Contract DAMD17-85-C-5200. These resins were being evaluated for use in a safe and effective skin decontamination system.

Rohm and Haas developed five in vitro test methods related to either the sorptive or reactive capacity of the candidate resins. These test methods are:

1. Static capacity
2. Contract desorption
3. Liquid phase sorption
4. Vapor desorption
5. Reactive capacity

The data obtained from testing resins and resin formulations with both chemical surety material (agents) and agent simulants can be used to rank order unformulated resins with respect to their effectiveness in a skin decontamination system and to determine the effect of the addition of excipients on resin performance. This data base will also provide a characterization of the resin formulation selected for use in the field-tested skin decontamination system.

During the first phase of this effort MRI was adapting Rohm and Haas test protocols for use with chemical surety agents. A brief description of each of the test methods including objective, experimental parameters, test modifications (necessitated by surety regulations or arising from evaluation of preliminary test results) and problem areas was presented in the 1986 Annual Report[1].

On the basis of results from preliminary tests carried out during this phase, it was decided that the Static Capacity Test would be eliminated from the Phase II test design.

[CCl_4 was used in the simulant testing. Agent volatility is too low for equilibration in a reasonable time.]

Prior to proceeding with Phase II, in which resin test protocols would be validated, Rohm and Haas prepared a new lot of resins by a modified grinding procedure and results from their

simulant testing indicated that Phase I results would not relate to data obtained for the newly prepared material. Therefore, Phase I data have not been included in this report but are available in the Annual Report[1]. Section II contains the results and discussion relating to Phase II testing of resin lots designated XE-519, XE-521, (Ambergard) XE-555, and (Ambergard) XE-556 resins, which were prepared in August 1986.

b. Results and Discussion

(1) Contact Desorption Tests - One hundred milligram portions of Rohm and Haas resins XE-519, XE-521, (Ambergard) XE-555 and (Ambergard) XE-556 resins were contaminated with 15 µL of GD, HD, and VX, and these mixtures were placed in contact with M-8 paper in test vials. The test vials were incubated at three temperatures (37°C, ambient (about 25°C), -35°C). Observations to detect an M-8 paper color change were made at 3, 6 and 24 hours.

A review of the Contact Desorption Test data led to questions with regard to the positive color changes observed for GD and HD incubated at -35°C. It was determined that the protocol required modification so that all materials were equilibrated at -35°C before contact was made between contaminated resin and M-8 paper.

Neat agent experiments were run with the modified test procedure and the results are described as follows:

GD (100 µL) - Paper wetted but no color change observed. A 4 hour test vial was warmed to ambient temperature and a gold color, indicating a positive, test was observed.

HD (30 µL) - Agent froze. Paper was not wetted and no color change was observed. A 4-hour test vial was warmed to ambient temperature and a pink color, indicating a positive test, was observed.

VX (100 µL) - Paper was wetted but no immediate color was observed. At 1 hour a blue ring appeared at the periphery of the wetted area. By 4 hours the remainder of the wetted area had slowly turned blue.

It appears that M-8(1) paper reaction with agent equilibrated at -35°C would not be appropriate for monitoring desorption of GD or HD. Resins contaminated with VX could be compared with no resin controls but it should be determined if the 1-hour observation of color with neat agent would vary with amount applied.

Therefore, only the results of ambient and +37°C test are

discussed below. The summary below applied to the data obtained for challenges at 1X the use level. (15-µL results in Tables 23 through 25).

(3-hour results)

1. No color change was observed for any resin at any temperature at the 3 hours.

(6-hour results)

2. At 6 hours there was still no observation of a color change indicative of GD liquid. A positive HD response was seen for one of three replicates of XE-519 at 37°C and one of three replicates of XE-555 at room temperature at 6 hours. All other HD test vials continued to show no color change that would indicate the presence of HD liquid.

   At 37°C only Resins 519 and 521, contaminated with VX produced a positive test at 6 hours, while VX-contaminated XE-555 and XE-556 were still not reacting with M-8 paper at 6 hours.

(24-hour results)

3. At 24 hours there continued to be no M-8 paper color change for GD.

   All HD test vials were also negative except the two positive samples previously observed at 6 hours.

   After 24 hours only VX-contaminated resin XE-519 incubated at room temperature was showing no color change for all three replicates.

In summary, it would appear that the Rohm and Haas resins tested retain the liquid contamination for all three agents for up to 6 hours. This performance level continues for up to 24 hours for resins contaminated with agents GD and HD, while VX-contaminated resins begin to give positive liquid agent responses with M-8 paper. For those contaminated resins that showed no color change after 24-hour contact with M-8 paper, further tests with increasingly higher agent concentrations were performed. These data are given in Tables 23 through 25.

In these data tables some temperature effects can be observed for tests run with VX and GD. At 37°C and 20 µL GD all resins showed desorption at 24-hour observation while XE-519 and XE-555 showed no color change when tested with 20 µL GD at room temperature. These GD results also demonstrate a difference between XE-519, Ambergard XE-555 resin, and XE-521, Ambergard XE-556, resin when the 1X use level is exceeded. Table 25 shows that all resins desorbed VX (dosed at 2X use level) more quickly at the higher temperature.

Table 23

CONTACT DESORPTION, GD[a]

Resin	37°C						Room Temperature								
	15 µL			20 µL			15 µL			20 µL			30 µL		
	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr
XE 519	-	-	-	-	-	+									
	-	-	-	+						-	-	-	+		
	-	-	-	-	-	+				-	-	-	+		
										-	-	-	+		
XE 521	-	-	-	-	-	+									
	-	-	-	+			-	-	-	+			+		
	-	-	-	-	-	+	-	-	-	+			+		
							-	-	-	+			+		
XE 555	-	-	-	+											
	-	-	-	-	-	+				-	-	-	+		
	-	-	-	-	-	+				-	-	-	+		
										-	-	-	+		
XE 556	-	-	-	+											
	-	-	-	+			-	-	-	-	+		+		
	-	-	-	+			-	-	-	+			+		
							-	-	-	+			+		

a Resin amount was 100 mg.

Table 24

CONTACT DESORPTION, HD[a]

Resin	37°C						Room Temperature											
	15 µL			30 µL			15 µL			30 µL			40 µL			60 µL		
	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 h
XE 519	-	+		+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	+			+			+		
XE 521	-	-	-	+			-	-	-	-	+		+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	+			+			+		
XE 555	-	-	-	+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		
XE 556	-	-	-	+			-	+		-	+		+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		
	-	-	-	+			-	-	-	-	-	-	+			+		

a Resin amount was 100 mg.

Table 25

CONTACT DESORPTION, VX[a]

Resin	37°C						Room Temperature											
	15 µL			30 µL			15 µL			30 µL			45 µL			60 µL		
	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr	3 hr	6 hr	24 hr
XE 519	-	+		+			-	-	-	-	-	+	-	-	+	-	+	
	-	+		+			-	-	-	-	-	+	+			-	+	
	-	+		+			-	-	-	-	-	+	-	+		-	+	
XE 521	-	+		+			-	-	-	-	-	+	-	-	+	-	+	
	-	+	+	+			-	-	+	-	-	+	-	+		-	+	
	-	+		+			-	-	+	-	-	+	+			-	+	
XE 555	-	-	-	+			-	-	-	-	-	+	-	-	+	-	-	+
	-	-	+	+			-	-	+	-	-	+	-	+		-	-	+
	-	-	-	+			-	-	+	-	-	+	-	-	+	-	-	+
XE 556	-	-	-	+			-	-	+	-	-	+	-	+		-	-	+
	-	-	-	+			-	-	-	-	-	+	+			-	+	
	-	-	+	+			-	-	+	-	-	+	-	+		-	-	+

a Resin amount was 100 mg.

It should be noted that at the 1X use level the effect of temperature is not as conclusive and a larger population would be required to draw statistically significant conclusions.

(These results may, however, suggest that if an increase in desorption with increasing temperature exists, the increase is not extremely large.)

(2) Liquid Sorption Tests - The rate at which Rohm and Haas resins sorb neat liquid agent was determined with the use of a modified Enslinn apparatus. Uptake was measured by observing the travel of the meniscus along an agent-filled glass capillary tube after contact was made with a bed of resin. The results are summarized (in Table 26).

(Table 26)

Liquid Sorption of Ambergard Resins with GD, HD and VX

Resin	Liquid Uptake Rate (s/mL x 100)		
	GD	HD	VX
XE-519	5.44 ± 0.68	5.03 ± 0.58	13.35 ± 1.20
XE-521	4.31 ± 0.55	4.69 ± 0.49	12.68 ± 1.21
XE-555	6.19 ± 0.31	5.56 ± 0.19	15.61 ± 1.66
XE-556	4.71 ± 0.43	5.18 ± 0.32	15.07 ± 2.34

If this test accurately reflects the resins' ability to remove liquid agent contamination from a surface, the tested materials will work approximately three times as well for both GD and HD as for VX.

(Some effect is likely, but the rubbing (mixing) may cause a leveling effect which would reduce these differences in the real world. The reduced efficacy for VX in the in vivo tests, reported in Section F, is not considered to be a result of slow sorption.)

(3) Reactive Capacity Tests - The Rohm and Haas resins are designed to decontaminate a surface by two complementary mechanisms: sorption and degradation. Reactive Capacity Tests were performed by adding a sufficient quantity of agent to saturate the sorptive sites so that the amount of unrecovered agent would be solely attributable to agent destruction. That is, at the point at which an increase in the agent/resin ratio effected no change in the amount of unrecovered agent after 24 hours, both the sorptive and reactive capacities would be considered saturated. Then the unrecovered agent value would be used in the determination of reactive capacity (meq of agent destroyed/g resin).

Agent challenges to 100-mg portions of resin were 60, 90, 105 and 120 µL, or 4X, 6X, 7X, and 8X the defined use level. For both agents GD and HD, the amount of unrecovered agent continued to increase as the contamination level increased from 4X to 8X. Since testing was to be terminated at eight times the use level, reactive capacities as defined above could not be calculated for resins contaminated with either GD or HD.

(This catalytic-type effect was not seen with simulants, and is a very positive result. As reported in the 1986 Annual Report[1], GD dose levels of nearly 200% of resin weight were used and were essentially all destroyed.)

As shown in Table 27, resin reactive capacities for the agent (VX results) were determined for XE-519 and (Ambergard) XE-555 (resin) and equivalent calculations were performed for XE-521 and (Ambergard) XE-556 (resin) for comparison purposes, even though the values were still increasing with those at the 6X level (90 µL) for these two blended resins.

It was not possible to determine reactive capacities as defined above for all agent-resin combinations. However, a summary of unrecovered agent at 4X the use level and values (approximating agent destroyed) for a 24-hour exposure at 27°C is provided in Table 28 for the purpose of making rough performance comparisons.

A follow-up experiment was designed to investigate why more than 90% of HD and of VX was recovered in these tests, while only 10% of the applied GD was recoverable.

Resin XE-519 was subjected to a dry nitrogen stream for 24 h in an effort to reduce the moisture content. This sample was then contaminated with 60 µL of GD and incubated for 24 h at 27°C. The test results given in Table 29 show that the moisture content reduction drastically reduced the reactive capacities for GD.

When the amount of milliequivalents of GD destroyed by the aerated sample of XE-519 is compared with HD and VX values for non-aerated resin, a striking similarity is observed. This may suggest that the ability of resins to degrade agents (independent of moisture content) is essentially the same for all three agents tested.

(While the above argument may be valid, the "old" resins evaluated in Phase I by MRI showed the same high reactivity toward GD. The moisture content of these old resins was only about 10% (new grindings are above 30% moisture). Thus, a significant drying of the current resins could occur without a corresponding loss in efficacy.)

Table 27

VX REACTIVE CAPACITY DETERMINATIONS AT 27°C

Resin	Challenge Volume (μL)	VX Destroyed (mg)	Reactive Capacity (meq/g)
XE 519	60	4.4	0.16
	90	4.6	0.17
XE 521	60	5.7	0.21
	90	8.4	0.31
XE 555	60	6.8	0.25
	90	4.4	0.16
XE 556	60	5.5	0.21
	90	8.9	0.33

Table 28

SUMMARY OF UNRECOVERED AGENT FROM 100 mg OF RESINS CONTAMINATED FOR 24 HR AT 27°C WITH FOUR TIMES THE USE LEVEL (60 µL)

	GD			HD			VX		
	mg	meq	%[a]	mg	meq	%	mg	meq	%
XE-519	54	0.30	88	4.4	0.028	5.8	4.4	0.016	7.3
XE-521	54	0.30	88	3.9	0.025	5.1	5.7	0.021	9.4
XE-555	56	0.31	92	5.3	0.033	7.0	6.8	0.025	11
XE-556	55	0.30	90	5.2	0.033	6.8	5.4	0.021	8.9

[a] Percent of total applied agent.

Table 29

SUMMARY OF 24-HR REACTIVE CAPACITY DATA FOR RESIN XE-519 AT 27°C AND 4X USE LEVEL

Agent (60 µL)	Resin (100 mg)	Unrecovered Amounts of Agent		
		mg	meq	%
GD	XE-519	54	0.30	88
GD Aerated	XE-519	3.6	0.020	5.9
HD	XE-519	4.4	0.028	5.8
VX	XE-519	4.8	0.016	7.3

When the reactive capacity protocol was carried out at -35°C and the 6X use level for all agents and resins, a substantial reduction of agent degradation was observed. These data are given in Table 30. Elevated temperature tests (+37°C) were run only with agent VX, and the general trend was to recover less agent at elevated temperatures than in runs at room temperature. One can, therefore, assume that the reactive capacity increases with increases in temperature.

(4) Vapor Desorption Tests - All four resins were challenged at 4X the use level 60 µL/100 mg) with GD, HD, and VX and were incubated at 37°C for 24 hours. The desorbed vapor and retained liquid were measured at the end of the test period. The amount of destroyed agent was calculated by taking the difference between the applied amount and the sum of the two measured amounts. The data from these tests are summarized in Table 31.

The comparison of resin data with the data for a no-resin control at this high challenge concentration indicates that although 5-30 times more agent is destroyed in the presence of resin, the amount of desorbed vapor was not significantly affected except in the case of GD tests. This would indicate that the sorptive capacity of the 100 mg of resin was exceeded by 60 µL of agent.

A comparison in Table 32 of the amount of GD destroyed during these Vapor Desorption Tests with that destroyed during the Reactive Capacity Test further supports the theory that resin moisture content plays a significant role in the destruction of GD.

Vapor Desorption Tests were run at the use level for agents HD and GD (15 µL agent/100 mg resin). VX was not included in this series of tests because the amount of vapor collected during the 4X test was near the detection limit, and it was decided that no useful information would be obtained from testing VX at the 1X use level.

The 1X tests were run at three temperatures (37°C, 25°C, and -35°C), and the data are presented in Tables 33 and 34. When operating at 1X the use level, the presence of resin reduced the amount of collected vapor by as much as two orders of magnitude with respect to the no-resin controls and desorbed agent was not seen to increase when the temperature increased from 27°C to 37°C.

Table 30

24-HR RESIN REACTIVITY TEST RESULTS

Liquid Challenge Volume (μL)	Temp. (°C)	GD Destroyed (mg)[a] XE 519	XE 521	XE 555	XE 556
60 - 4X use level	+27	54	54	56	53
90 - 6X use level	+27	87	86	93	86
	-35	4.3	2.7	6.7	5.5
105 - 7X use level	+27	110	115	110	110
120 - 8X use level	+27	120	130	120	130
	-35	1[illegible]	0	0	2

Liquid Challenge Volume (μL)	Temp. (°C)	HD Destroyed (mg)[a] XE 519	XE 521	XE 555	XE 556
60 - 4X use level	+27	4.4	3.9	5.3	5.2
90 - 6X use level	+27	5.0	2.9	6.1	2.9
	-35	0	0	0	0
105 - 7X use level	+27	11	8.8	0.7 {7.5}[d]	7.7
120 - 8X use level	+27	15	1.6 ((7.6))[e]	14	15
	-35	0	0.3	0.3	0

Liquid Challenge Volume (μL)	Temp. (°C)	VX Destroyed (mg)[a] XE 519	XE 521	XE 555	XE 556
60 - 4X use level	+27	4.4	5.7	8.8	5 -
90 - 6X use level	+27	15 (26)[b]	2.0 [[7.3]][f]	21 [26][c]	25
	+27	4.6	8.4	4.4	15.- [3 9][c]
	-35	2.1 (13)[b]	0 [[2.2]][f]	22 [17][c]	5 8

a Difference of recovered agent at zero-time and 24 hr.

b Zero-time % recovery for this run was 85%. Numbers in (parentheses) are calculated on basis of mean recovery, x ± S.D.; 96 ± 6.

c Zero-time % recovery for this run was > 100%. Numbers in [brackets] are calculated on basis of mean recovery, x ± S.D.; 96 ± 6.

d Agent destroyed data are based on mean of duplicate 24-hr recoveries (126.6 and 140.3 mg). Since 140.3 mg exceeds zero-time recovered HD, HD destroyed was recalculated on basis of 126.6 mg only. This number is given in {braces}.

e Zero-time % recovery for this run was 94%; value in ((double parentheses)) is a recalculation based on mean % recovery of 97%.

f Zero-time % recovery for this run was 91%; value in [[ ]] is a recalculation based on mean % recovery of 97%.

Table 31

AGENT DISTRIBUTION IN VAPOR DESORPTION TESTS AT 37°C WITH DOSAGE AT 4X USE LEVEL (60 µL AGENT/100 mg RESIN)

Resin	Recovered Agent (mg)						Destroyed Agent[a] (mg)		
	Collected Vapor			Retained Liquid					
	GD	HD	VX	GD	HD	VX	GD	HD	VX
No resin	48	11	0.20	12	54	61	1.5	0.15	1.6
XE 519	25	12	0.50	7.2	48	56	29	9.6	6.6
XE 521	29	14	0.15	9.0	52	56	22	9.2	6.6
XE 555	23	11	0.15	7.9	46	56	30	8.0	6.1
XE 556	24	9.6	0.10	10	43	53	27	8.6	8.2

[a] Destroyed agent = difference of applied amount - (collected vapor + retained liquid).

Table 32

COMPARISON OF AMOUNTS OF GD DESTROYED IN REACTIVE CAPACITY AND VAPOR DESORBTION TESTS

	MG GD Destroyed	
	Desorption Test Data[b]	Reactive Capacity Test Data
No resin	1.5	1.1
519	29	54 (3.6)[a]
521	22	54
555	30	56
556	27	55

[a] Aerated 519.
[b] Aeration part of test protocol.
[c] No aeration in this protocol.

Table 33

AGENT DISTRIBUTION IN VAPOR DESORPTION TEST AT THREE TEMPERATURES (37, 25, -35°C) WITH GD DOSAGE AT 1X USE LEVEL (15 µL/100 mg RESIN)

Temperature	Resin	Collected Vapor (mg)	Retained Liquid (mg)	Destroyed Agent[a] (mg)
37°C	No resin	14	ND[b]	1.3
	XE 519	0.10	1.9	14
	XE 521	0.10	3.8	12
	XE 555	0.10	1.8	14
	XE 556	0.15	3.0	13
25°C	No resin	16	ND	0.05
	XE 519	0.10	6.0	10
	XE 521	ND	6.6	9.6
	XE 555	0.10	6.4	10
	XE 556	0.20	7.1	9.2
-35°C	No resin	0.60	16	0.30
	XE 519	0.10	15	1.8
	XE 521	0.10	14	3.2
	XE 555	< 0.10[c]	13	3.4
	XE 556	< 0.10	12	4.0

a Agent destroyed = applied amount - (collected vapor + retained liquid).
b ND = no response detected.
c Visible response but less than lower limit of quantitation, 0.10 mg.

Table 34

AGENT DISTRIBUTION IN VAPOR DESORPTION TEST AT THREE TEMPERATURES (37, 25, -35°C) WITH HD DOSAGE AT 1X USE LEVEL (15 µL/100 mg RESIN)

Temperature	Resin	Collected Vapor (mg)	Retained Liquid (mg)	Destroyed Agent[a] (mg)
37°C	No resin	11	7.0	0.60
	XE 519	0.20	11	4.6
	XE 521	0.35	12	3.9
	XE 555	0.20	12	4.3
	XE 556	0.30	12	4.2
25°C	No resin	4.0	13	0
	XE 519	0.20	12	3.8
	XE 521	0.25	13	3.3
	XE 555	0.20	13	3.8
	XE 556	0.30	13	3.7
-35°C	No resin	ND[b]	16	0.10
	XE 519	ND	15	1.0
	XE 521	ND	15	0.75
	XE 555	ND	16	1.0
	XE 556	ND	16	0.35

a Agent destroyed = applied amount - (collected vapor + retained liquid).
b ND = no response detected.

c. Summary

In summary, the results of chemical surety testing done at MRI on Rohm and Haas resins show the largest differences in performance between agents rather than between the four resins. Generally, the addition of excipients had little effect on test responses. (This is an indication that the careful selection of excipients chosen was successful in preventing efficacy loss). The effect of increasing temperature enhanced resin performance for the reactive tests but may have slight adverse effect on the contact desorption performance. When testing with GD, the resin moisture content is critical to the amount of agent degradation observed.

3. Comparison of MRI Agent Data to Rohm and Haas Simulant Data

The same lots of XE-519, XE-521, Ambergard XE-555 and Ambergard XE-556 resins that were evaluated at MRI were evaluated at Rohm and Haas using simulants. One of the reasons for including the chemical surety effort in the program was to validate the simulant work. This section is included to compare these data.

a. Contact Desorption Test

The Contact Desorption Test was run at elevated and cold temperatures on XE-519, XE-521, Ambergard XE-555 resin, and Ambergard XE-556 resin with DFP and CIS. No VX simulant was available. These results are summarized in Tables 35 and 36. MRI's agent data are shown in the preceding section Tables 23, 24 and 25. The "use levels" (agent dose about 15% of resin weight) are 25 µL for simulant data and 15 µL for agent data, owing to the different resin weights used.

Comparing, first, the DFP and GD data (Tables 35 and 23), no desorption is seen for either challenge at the 1X level, and both challenges show desorption at the room temperature 2X level. No 2X data are reported for GD at 37°C.

Table 35

Contact Desorption Test with DFP at Various Temperatures

Resin[a] Lot	37 °C						25 °C					
	25 µL			50 µL			25 µL			50 µL		
	3	6	24 h	3	6	24 h	3	6	24 h	3	6	24 h
XE-519	-	-	-[b]	+			-	-	-	+		
ND0537	-	-	-	+			-	-	-	+		
	-	-	-	+			-	-	-	+		
XE-521	-	-	-	+			-	-	-	+		
ND0538	-	-	-	+			-	-	-	+		
	-	-	-	+			-	-	-	+		
XE-555	-	-	-	+			-	-	-	+		
EOJ3795A	-	-	-	+			-	-	-	+		
	-	-	-	+			-	-	-	+		
XE-556	-	-	-	+			-	-	-	+		
EOJ3795B	-	-	-	+			-	-	-	+		
	-	-	-	+			-	-	-	+		

Table 36

Contact Desorption Test with CIS at Various Temperatures

Resin[a] Lot	37 °C						25 °C					
	25 µL			50 µL			25 µL			50 µL		
	3	6	24 h	3	6	24 h	3	6	24 h	3	6	24 h
XE-519	-	-	-[b]	-	-	-	-	-	-	-	-	-
ND0537	-	-	-	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-	-	-	-
XE-521	-	-	-	+			-	-	-	+		
ND0538	-	-	-	+			-	-	-	+		
	-	-	-	+			-	-	-	+		
XE-555	-	-	-	-	-	-	-	-	-	+		
EOJ3795A	-	-	-	-	-	-	-	-	-	+		
	-	-	-	-	-	-	-	-	-	+		
XE-556	-	-	-	-	-	-	-	-	-	+		
EOJ3795B	-	-	-	-	-	-	-	-	-	+		
	-	-	-	-	-	-	-	-	-	+		

[a] All resin amounts were 0.17 g.
[b] "-" indicates no response and "+" indicates a response on M-8 paper.

Both CIS and HD show no desorption at the 1X level at room temperature or 37°C. The good agreement ends there. However, the results do indicate that generally CIS and HD are less easily desorbed than DFP and GD. The desorption observed when using 50 µL CIS after only 3 h at 25°C is difficult to explain in view of the lack of desorption after 24 h at both 0°C and 37°C. A similar trend is not observed with HD. It is possible that a sharp threshold exists at which only a very small difference in the relative amount of simulant to resin can result in a positive or negative response. This explanation is not very satisfying considering the good reproducibility between replicates.

b. Liquid Sorption Test

The Liquid Sorption Test is not easily thermostated to evaluate temperature differences. The data reported in MRI's report are all at ambient temperature. Simulant data are reported in Table 37. Only diethyl malonate was used (GD simulant). The results are reported as time to end point. As mentioned in the test development section, direct comparison of rates on two different apparatus is not possible. The ranking of the resins is the same for GD as for diethyl malonate. As reported in the 1986 Annual Report[1], similar rates were observed for diethyl malonate and methyl salicylate (HD simulant). The similarity in rates seen by MRI between GD and HD and the large difference with VX suggest the need to evaluate a simulant with physical properties similar to those of VX.

Table 37

Liquid Sorption Results on Mechanically Ground Resins with Diethyl Malonate

Resin	Lot	Time to Mark #5	Standard Deviation	N
XE-519	ND0537	19.2650	1.44010	4
XE-521	ND0538	18.0675	1.52775	4
XE-555	EOJ3795A	22.1925	2.47075	4
XE-555	EOJ3795A	23.7600	1.21579	4
XE-556	EOJ3795B	21.8150	0.95668	4

c. Reactive Capacity Test

The Reactive Capacity Test was run at room temperature and at 37°C with DFP and CIS. These data are shown in Tables 38 and 39. Agent data are shown in Tables 27 through 30. The only direct comparison generalization that can be made is that the reactive capacity increases with temperature. This is likely due, to significant degree, to thermal decomposition of the simulant.

Table 38

Reactive Capacity Measurements on Candidate Resin Systems

Resin	Lot	DFP Reactive Capacity meq/g	Standard Deviation	CIS Reactive Capacity meq/g	Standard Deviation
XE-519	ND0537	0.42	0.03	0.86	0.04
XE-521	ND0538	0.28	0.03	0.81	0.01
XE-555	EOJ3795A	0.38	0.02	0.86	0.03
XE-556	EOJ3795B	0.26	0.03	0.87	0.01

Table 39

Reactive Capacity Measurements on Candidate Resin Systems at 37°C

Resin	Lot	DFP Reactive Capacity meq/g	Standard Deviation	CIS Reactive Capacity meq/g	Standard Deviation
XE-519	ND0537	1.44	0.06	1.54	0.02
XE-521	ND0538	1.23	0.12	1.65	0.07
XE-555	EOJ3795A	1.35	0.85	1.52	0.04
XE-556	EOJ3795B	1.35	0.06	1.55	0.03
No Resin Blank[a]		0.47		0.64	

[a] Calculated value based on 24-h thermal decomposition assuming 0.10 g of resin.

The MRI data show that the resin systems are much more reactive toward GD and HD than DFP and CIS. While it is well documented that the hydrolysis rates for GD and HD are much faster than for the corresponding simulants, it was gratifying to note that a significant increase in the capacity was also observed.

d. Vapor Desorption Test

Vapor Desorption Test results with simulants DFP and CIS at various temperatures are shown in Tables 40 and 41. The simulant dose is 50 µL in all cases; thus 0.34 g and 0.17 g of resin represent 1X and 2X levels, respectively. The live-agent data are shown in Tables 31 and 33. Table 31 shows the desorption data for all three agents at the 4X level at 37°C. Simulant data were not obtained at this level and thus no direct comparison is possible. As MRI reports, the resin capacity for

VX and HD is likely exceeded, resulting in the "no resin" results being similar to the resin results.

Table 33 shows the GD data at various temperatures at the 1X use level. These data do not agree well with the DFP data in Table 40. The high reactivity of the GD may account for much of this difference.

Table 40

Vapor Desorption Measurements on Candidate Resin Systems with DFP

Resin	Temp °C	Weight g	% Desorbed	% Retained	% Lost
Blank	0	0.00	3.00	87.80	9.20
XE-555	0	0.17	1.35	86.60	12.05
Blank	23	0.00	11.90	82.20	5.90
XE-555	23	0.17	8.15	83.10	8.75
XE-556	23	0.17	5.70	81.85	12.45
Blank	37	0.00	48.06	44.41	7.53
XE-519	37	0.17	18.65	61.10	20.25
XE-521	37	0.17	20.70	55.00	24.30
XE-555	37	0.17	22.35	58.20	19.45
XE-555	37	0.34	9.65	69.50	20.85
XE-556	37	0.17	24.20	51.75	24.05
XE-556	37	0.34	15.25	61.60	23.15

Table 41

Vapor Desorption Measurements on Candidate Resin Systems with CIS

Resin	Temp °C	Weight g	% Desorbed	% Retained	% Lost
Blank	0	0.00	2.00	98.00	0.00
XE-555	0	0.17	1.60	97.75	0.65
Blank	23	0.00	8.80	81.95	9.25
XE-555	23	0.17	7.35	69.85	22.80
XE-556	23	0.17	4.25	73.30	22.45
BLANK	37	0.00	32.93	58.51	8.56
XE-519	37	0.17	18.55	54.55	26.90
XE-521	37	0.17	19.50	55.95	24.55
XE-555	37	0.17	16.95	48.95	34.10
XE-555	37	0.34	8.60	55.15	36.25
XE-556	37	0.17	20.05	49.85	30.10
XE-556	37	0.34	6.30	52.80	40.90

e. Summary

While certain trends are noted between the agent data and the simulant data, similar results are not always seen. In general, agent data and simulant data give the same rank-ordering of resins, but not the same absolute numbers.

Fortunately, in nearly every case, the data suggest that the resins perform better against agents than the corresponding simulants. This is especially evident in the reactivity tests. Simulant data indicate that reactivity is minimal, owing to preferential sorption of the simulants on the sorptive components. The MRI data clearly indicate that the resins are very effective at destroying GD.

4. Additional In Vitro Testing

a. Vapor Phase Desorption Tests on Accelerated Stability Samples

(Vapor phase desorption testing of these samples was prompted as a result of the testing performed with simulants on these same resins. In the simulant tests, a decrease in desorption was observed for the samples stored at elevated temperatures, a desirable although unexpected effect. Prior to MRI's evaluation, the samples had been stored for approximately 18 months at ambient conditions and 1 year at the indicated accelerated storage temperatures.)

Samples of Ambergard XE-519 resin (EOJ3567), stored by Rohm and Haas for one year at ambient temperature and at 40°C and 60°C, were tested with agent soman at the 1X and 2X use levels and with agent HD at the 1X use level. The following quality control samples were included in the sample set:

Dose control: Agent challenge volume dispensed into extraction solvent and analyzed with no further treatment

No resin control: Agent challenge volume dispensed into first impinger of empty vapor desorption train, which is then treated in the same fashion as a resin sample train

Time = 0 extraction efficiency sample: Agent challenge volume dispensed onto resin and extracted immediately

The agent recovered value for T = 0 is provided in the data tables, but was not used in any of the calculations to adjust values for extraction efficiency.

The results for GD tests are summarized in Table 42. At both challenge levels, the amount of desorbed vapor was equivalent for ambient and 40°C samples and 2 to 3 times greater for the 60°C sample. The liquid retained by the resins exhibited

Table 42

Accelerated Stability Samples - Vapor Desorption Tests: GD
T = 24 h

1X Challenge Dose Controls
N = 8, X = 15.1 ± 0.2 mg

Vapor Collected (mg)			
No Resin	Ambient	40°C	60°C
15.0	0.1	0.1	0.4
14.5	< 0.1	0.1	0.2
14.5	< 0.1	-	-
14.0	< 0.1	-	-

Liquid Retained (mg)			
No Resin	Ambient	40°C	60°C
< 0.1	10.3	9.4	13.2
< 0.1	10.2	9.6	13.9
< 0.1	8.3	-	-
< 0.1	8.6	-	-
T = 0	14.1, 13.4	13.9	15.2

Agent Not Recovered (Destroyed)			
No Resin	Ambient	40°C	60°C
0.3	4.9	5.6	1.6
0.7	5.1	5.4	1.1
0.3	6.7	-	-
1.0	6.4	-	-

2X Challenge Dose Controls
N = 4, X = 29.8 ± 0.5 mg

Vapor Collected (mg)			
No Resin	Ambient	40°C	60°C
22.4	4.3	4.9	8.5
26.1	3.8	5.7	8.9
-	3.5	-	-
-	3.6	-	-

Liquid Retained (mg)			
No Resin	Ambient	40°C	60°C
6.4	13.5	14.5	19.2
3.0	13.8	14.1	17.8
-	13.0	-	-
-	14.0	-	-
T = 0	28.2, 27.2	28.4	30.2

Agent Not Recovered (Destroyed)			
No Resin	Ambient	40°C	60°C
1.8	12.8	10.0	2.9
0.3	13.0	9.6	3.9
-	12.9	-	-
-	11.8	-	-

the same trend (i.e. ambient and 40°C samples retaining equivalent amounts of liquid agent and the 60°C sample retaining 40% more agent). Since the "agent destroyed values" are calculated by subtracting recovered agent from applied agent, the 60°C samples have less agent destroyed, which may be because of a diminished reactive capacity.

(These results suggest a significant decrease in reactive capacity with GD for the 60°C samples. (Similar simulant data described in preceding Section B.4, on the other hand, revealed only a slight decrease in reactivity with (DFP). Also, there was an increase in the amount of GD desorbed for the 60°C sample over the ambient and 40°C samples. (With DFP, a decrease in desorption was observed.) A significant loss of reactivity for the 40°C sample was not observed.)

The (mustard) HD data are given in Table 43. Only resins stored under ambient temperature and at 60°C were evaluated. The 60°C samples retained slightly more liquid agent than the ambient samples. This difference is reflected in the agent destroyed data as a reduction of reactive capacity. More replicates would be required to determine whether or not the vapor desorbed data for the two sample sets were significantly different from one another.

Table 43

Accelerated Stability Samples - Vapor Desorption Tests - HD
T = 24 h

1X Challenge Dose Controls
N = 4, X = 19.5 ± 0.4 mg

Vapor Collected (mg)		
No Resin	Ambient	60°C
1.9	0.2	0.5
-	0.1	0.1

Liquid Retained (mg)		
No Resin	Ambient	60°C
15.0	14.4	16.8
-	14.6	16.7

Agent Not Recovered Destroyed (mg)		
No Resin	Ambient	60°C
3.2	5.5	2.8
-	5.6	3.3

(A slight decrease in reactivity and no change in desorption were seen with the HD simulant data, chloroethyl isobutyl sulfide (CIS). The volatility of HD is too low to make any comparisons of vapor desorption between CIS and HD. Again, MRI's agent results suggest a significant decrease in reactive capacity of the 60°C accelerated storage sample after 1 year.)

b. Vapor Phase Desorption from Cold Samples

A new protocol was developed especially for cold samples, to simulate the most likely use situation. Agent was dispensed into an impinger and allowed to come to equilibrium at -35°C. Resin stored for 24 hours at -35°C was added and mixed with the -35°C agent. The spiked impinger was then attached to the vapor desorption train and the gas flow was initiated. The cold agent/resin mixture was allowed to warm to 25°C as the testing proceeded. Quality control samples included all of those

discussed in Section E.2, except the no resin control samples. The GD challenge was 1X use level. No HD challenge was requested.

The GD vapor desorption test data for samples run at ambient temperature (about 27°C) and at reduced temperature following the modified protocol were not significantly different. The results are presented in Table 44.

Table 44

Effect of Temperature on GD Vapor Desorption

Resin: Ambergard XE-555 (Union Processing)
EOJ3936B, 2/13/87

Challenge: 1X Use Level
Dose Controls at Room Temperature:
N = 2, 15.2 mg
Dose Controls at -35°C:
N = 3, 15.2 mg

Vapor Collected (mg)	
-35°C	Room Temperature
0.5	0.2
0.3	0.3

Liquid Retained (mg)	
-35°C	Room Temperature
5.8	5.1
5.8	6.0

Agent Not Recovered (mg)	
-35°C	Room Temperature
8.9	9.9
9.1	8.9

(While vapor desorption tests at low temperatures are not meaningful, because of the low agent volatility, these tests were run to evaluate the effect of contaminated resin warming to room temperature and possibly off-gassing more agent than the resin would have if the mixing had occurred at milder temperatures. It is not surprisingly that no decrease in resin performance was observed. Blank (no resin) controls do show significant desorption under similar conditions (see Table 42), and

presumably had the agent not been sorbed into the resin, an increase in the vapor collected would have been observed.)

c. Vapor Phase Desorption from Union Process-Ground Resins

Duplicate 100-mg quantities of Union Process Ambergard XE-555 (EOJ3936) and Wedco Ambergard XE-555 (EOJ3795) resins were challenged with GD at 1X use level at 25°C for 24 hours. (The Union Process and Wedco designations refer to the method of grinding employed in the preparation of Ambergard XE-555 resin.)

The amounts of desorbed GD vapor collected from Wedco- and Union Process-ground Ambergard XE-555 resins were not significantly different. However, more liquid agent was recovered from the Wedco resin. These results would indicate that the freshly ground Union Process resin has a higher reactive capacity for GD. The data are summarized in Table 45.

Table 45

Comparative GD Vapor Desorption of Ambergard XE-555 Prepared at Union Process and at Wedco

1X Challenge Dose Control: 15.1 ± 0.2 mg

	Vapor Collected	Liquid Retained	Agent Not Recovered (Destroyed)
Ambergard XE-555	0.1	8.2	6.5
Wedco EOJ3795A 8/6/86	0.1	8.3	6.4
		T = 0: 13.0[a]	
Ambergard XE-555	0.4	5.2	9.2
Union Process EOJ3936B 2/13/87	0.1	4.8	9.9
		T = 0: 13.4[a]	

[a] T = 0 represents extraction efficiency

(The Wedco-ground material is the resin that was used in all of MRI's agent testing reported in the 1986 Annual Report[1]. The Union Process ground resin is the actual resin used in the prototype kits and used by Battelle MREF for the in vivo testing. These tests were run to see whether or not any significant difference between the two grindings existed. The difference observed, that of a higher reactivity, is certainly desirable. Some caution must be exercised in comparing the two results, as the Wedco material was evaluated 6 months ago and not rerun as a control in this experiment.)

d. Reactivity on Aerated XE-519

A sample of resin XE-519 (same lot used for GD aeration studies) was aerated under 100 mL/min nitrogen flow for 24 hours. One-hundred-milligram samples were placed in screw-cap tubes, dosed with 60 ul of HD and stored for 24 hours at 27°C. Nonaerated resin also was tested for comparison purposes. The quality control samples consisted of three no resin controls and a dose control.

Aeration of resin XE-519 for 24 hours caused only a slight reduction in the amount of HD destroyed as compared with nonaerated resin (6.4 vs. 8.5 mg). The data for GD destroyed by aerated resin versus nonaerated resin (5 mg vs. 61 mg) demonstrates that the mechanism of GD destruction is different and probably more dependent on moisture content than the degradation of HD. The HD results are given in Table 46.

Table 46

Effect of Aeration on Reactive Capacity for HD

100 mg Resin: XE-519
4X Challenge: 24 h at 26.5°C
No Resin Controls: N = 3, X = 78.3 ± 0.7

	Agent Recovered			Agent Not Recovered at 24 h
	T = 0	T = 24		
Untreated Resin	75.1	69.3		8.5
		69.3	X = 69.2 ± 0.1	8.5
		69.1		8.7
Aerated Resin	79.8	70.6		7.2
		73.7	X = 71.9 ± 1.6	4.1
		71.4		6.4

This page is intentionally blank.

F. IN VIVO CHEMICAL AGENT TESTING (ACTIVITY F)

1. Summary

Work performed under Activity F comprised the in vivo live-agent work conducted at Battelle Columbus Laboratories, Medical Research and Evaluation Facility (MREF). The in vivo testing at MREF was necessarily an iterative process of submitting samples, evaluation, and resubmission of samples. To facilitate the required rapid access to data, an agreement between MREF, USAMMDA, and Rohm and Haas was made allowing Rohm and Haas access to some data prior to full review by the MREF quality control unit. While the data will likely stand as reported below, MREF reserves the right to make corrections where necessary.

The in vivo testing conducted was divided into three sub-activities. Activity F.2 was designed to evaluate the efficacy of newly formulated resin systems, primarily to examine formulation excipient effects. Only TGD and HD were used as challenges. Activity F.3 was designed to examine the best formulations from Activity F.2 under more realistic dose amounts and application conditions. In addition to TGD and HD, VX was used as a challenge. Only XE-519 based resin systems were used in these initial tests. Final efficacy testing was performed under Activity F.4. Freshly ground and blended material was used for these F.4 tests. Both XE-519- and XE-521-based systems (Ambergard XE-555 and Ambergard XE-556 resins, respectively) were tested under Activity F.4. Five agents were used as challenges: GD, TGD, VX, HD, and L.

MREF Standard Protocols 21 and 22 were used to test against organophosphate and vesicant challenges respectively. Rohm and Haas provided the manufacturer's instructions for application of these resin systems.

2. Results and Discussion

a. Activity F.2

The primary objective under Activity F.2 was to demonstrate that any formulation excipients did not have a significant adverse effect on the efficacy of the resin systems. The fact that the unformulated resin systems had efficacy against CW agents was demonstrated under a prior contract, DAMD17-83-C-3071. We compared the formulated powders to the unformulated powder and the formulated creams to the unformulated suspension. The MREF protocols were designed to determine only if candidate materials are statistically as good as or better than the M258A1 kits. However, it was expected that any significant differences between formulated and unformulated resins would be evident. Only XE-519 formulations were included in this activity.

Doses and application procedures were kept similar to those in testing under the prior contract even though these did not represent reasonable end-use conditions. Our concern was that the resin systems might be "too good" if reasonable dosages were used and we would not be able to see any excipient effects. The conditions for F.2 testing used Battelle's protocol for "time to decon" and "rubbing time", a powder dose of 150 mg, 1.0 mL of the paste systems, a cotton swab for powder application, and a fiber fill pad to apply the paste systems.

Nine different resin systems were screened in Activity F.2. The data have been reported in the 1986 Annual Report[1]. The results of this testing weighed heavily on the selection of formulation excipients. This selection process is addressed in Section B.3 of this report. It will suffice here to identify the "best" formulations based on the data. These formulations are identified in Table 47 with the experimental number designations. The mineral oil formulations were dropped as a candidate non-aqueous system based on the poor protection against mustard.

Table 47

Summary of "Best" Formulations Based on Activity F.2 Tests

Resin Designation	RandH Lab ID	Formulation
XE-548	ND0472	Powder
XE-549	ND0474	Aqueous Cream
XE-550	DWH174	Nonaqueous Cream

b. Activity F.3

Our primary objective in Activity F.3 was to look at realistic application conditions against three agents; TGD, HD, and VX. The "best" cream formulations and the "best" powder formulations were carried into F.3. XE-519 was included in addition to the resins listed in Table 47 as a possible candidate decon material on its own.

The conditions for F.3 testing used: fiberfill heat-sealed to aluminum foil laminate to apply the powders and creams (simulating the foil pouch design); 0.75 g of powder and 2.0 mL of creams against TGD and VX and half these amounts against HD; and in addition to the specified rubbing times (10 s), rubbing times of half these values (5 s) for XE-548.

The data from this testing were reported in the Annual Report[1]. An overall summary is reported in Table 48. The test protocols were designed to determine whether candidate systems are statistically as good as or better that the M258A1.

Table 48

Summary of MREF Results Under Activity F.3 -
Efficacy of Candidate System Relative to the M258A1

Decon System	Decon Time	TGD	VX	HD
XE-519	10 s	Pass[a]	Fail[b,c]	Pass
XE-548	10 s	Pass	Fail	Fail[c]
XE-548	5 s	Pass	Fail	Pass
XE-549	10 s	Pass	Fail	Pass
XE-550	10 s	Fail	Fail	Fail

[a] Pass = as good or better than the M258A1.
[b] Fail = less effective than the M258A1.
[c] Some efficacy shown.

Again the mustard results indicated that a nonaqueous cream (XE-550) is not a viable system for decontamination of vesicants. The nonaqueous cream also performed poorly against both organophosphates. While all of the other formulations performed well against TGD, a large increase in efficacy was not seen when going from F.2 to F.3. In other words, the higher resin amounts and use of the fiberfill applicator did not result in a significant difference based on the in vivo data. The VX data results show all resin formulations to be less effective than the M258A1. Only the unformulated XE-519 demonstrates any efficacy against VX.

The lack of efficacy for VX and no significant increase of efficacy when using a larger amount of powder against TGD suggest that time to decon is the limiting factor when using a polymeric skin decontamination system. A plausible explanation for the VX data might be that the agent is so very toxic that even a very small quantity penetrating the skin prior to surface removal of any remaining agent is sufficient to sacrifice the rabbits. Similarly, with TGD, an increase in efficacy was not seen when using more resin because the lesser quantity was sufficient to remove any agent remaining on the skin surface. The greater quantity was in excess of the amount required. In the cases of both VX and TGD, whatever agent peretrated the skin surface could not be chased by a polymeric resin system.

Two points seem important here. First, we believe that the soft-pack packaging concept (see Section C) may allow for more rapid decon than the current kit. MREF Protocol 21 specifies a 2-min "time to decon." The criterion for selection of this time to decon was based more on the time required for the physical manipulations to safely dose and decontaminate the

rabbit in the laboratory than on the actual time required for field application. The resin systems may have significantly greater efficacy at more realistic shorter decon times.

The second issue centers on the validity of using animal models for skin penetration studies. This practice has long been a matter of controversy. There exist a substantial in vivo and in vitro data in the literature to suggest that skin permeation rates for rabbits are much faster than for human[7]. Obviously animals are the only practical means of performing in vivo agent studies. This issue remains outside the scope of this contract.

c. Activity F.4

The objectives under Activity F.4 were threefold.

First, a level of efficacy was to be determined against five threat agents: GD, TGD, VX, HD, and L. Protective ratios (PR) were to be determined for the organophosphates. As no protocol existed to establish a protective-ratio-type number for the vesicants, the resin systems were again evaluated relative to the M258A1 kit for HD and L.

A second objective was to include the XE-521-based formulation for the first time and to make a selection between the XE-519 and XE-521 systems based on the efficacy data.

A third objective was to use the actual freshly ground and formulated resin that was being prepared for the final prototypes.

All efficacy testing prior to Activity F.4 had been performed on resin prepared under contract DAMD17-83-C-3071. Changes in grinding techniques resulted in a resin having a higher moisture content and a higher hydroxide ion content, and requiring less formulation excipients to obtain the desired flow characteristics, as discussed elsewhere.

The conditions used for Activity F.4 were essentially the same as for Activity F.3 except the resin dose amounts were increased to 1.4 g to reflect the actual half-kit dose packaged in the final PCDS SDK (advanced development) prototypes.

The results for the F.4 testing are summarized in some detail in Tables 49 through 53.

Table 49

Summary of MREF Results with GD under Activity F.4

Median lethality values (LD_{50} in mg/kg) for topical application of GD on rabbits followed by decontamination with either nothing, M258A1 I and II, or one of two Rohm and Haas candidate decontamination system.

Treatment	N	LD_{50}	LL	UL	Slope ± 1 SE	PR
GD/None	160	1.35	0.93	1.7	3.87 ± 0.89	1.0
GD/M258A1 I & II	360	13.0	11.5	14.9	3.73 ± 0.52	9.6
GD/Ambergard XE-555 RESIN						
Replicate 1	78	14.0	8.9	18.0	2.80	
Replicate 2	80	14.3	11.9	17.5	4.25	
Replicate 3	198	14.1	12.3	16.1	3.49 ± 0.50	10.4
GD/Ambergard XE-556 RESIN						
Replicate 1	80	14.4	10.5	18.1	3.36	
Replicate 2	80	12.3	9.3	15.4	3.17	
Replicate 3	80	14.6	11.8	19.8	2.99	
Composite	240	13.6	11.8	15.5	3.14 ± 0.42	10.1

N = Number of rabbits
LL = Lower 95% confidence limit
UL = Upper 95% confidence limit
PR = Protective Ratio (LD_{50}-treated/LD_{50}-untreated)
SE = Standard Error

Table 50

Summary of MREF Results with TGD under Activity F.4

Median lethality values (LD_{50} in mg/kg) for topical application of TGD on rabbits followed by decontamination with either nothing, M258A1 I and II, or one of two Rohm and Haas candidate decontamination systems.

Treatment	N	LD_{50}	LL	UL	Slope ± 1 SE	PR
TGD/None	208	3.35	3.15	3.59	6.87 ± 1.18	1.0
TGD/M258A1 I & II	200	5.65	5.27	6.08	6.37 ± 0.99	1.7
TGD/Ambergard XE-555 RESIN						
Replicate 1	40	5.32	1.35	6.94	3.69	
Replicate 2	80	7.15	6.26	8.47	5.72	
Replicate 3	40	6.81	5.69	8.28	6.64	
Composite	160	6.67	6.05	7.37	5.41 ± 0.83	2.0
TGD/Ambergard XE-556 RESIN						
Replicate 1	80	6.41	5.42	7.16	6.24	
Replicate 2	80	6.64	5.47	8.05	7.76	
Replicate 3	40	5.90	1.40	7.56	4.56	
Composite	200	6.42	5.95	6.88	6.43 ± 1.00	1.9

N = Number of rabbits
LL = Lower 95% confidence limit
UL = Upper 95% confidence limit
PR = Protective Ratio (LD_{50}-treated/LD_{50}-untreated)
SE = Standard Error

Table 51

Summary of MREF Results with VX under Activity F.4

Median lethality values (LD_{50} in mg/kg) for topical application of VX on rabbits followed by decontamination with either nothing, M258A1 I and II, or one of two Rohm and Haas candidate decontamination systems.

Treatment	N	LD_{50}	LL	UL	Slope ± 1 SE	PR
VX (diluted 1:100)/None	136	0.031	0.020	0.103	2.73 ± 0.79	1.0
VX/M258A1 I & II	360	1.34	1.220	1.480	3.57 ± 0.41	43.2
VX/Ambergard XE-555 RESIN						
Replicate 1	79	0.812	0.396	0.994	5.79	
Replicate 2	40	0.995	0.479	1.260	4.24	
Replicate 3	87	0.647	0.467	0.763	4.10	
Composite	206	0.708	0.567	0.814	3.79 ± 0.64	22.8
VX/Ambergard XE-556 RESIN						
Replicate 1	80	0.625	0.446	0.864	4.46	
Replicate 2	120	0.492	0.076	0.729	3.19	
Replicate 3	80	0.446	0.297	0.557	3.05	
Composite	280	0.514	0.422	0.599	3.33 ± 0.67	16.6

N = Number of rabbits
LL = Lower 95% confidence limit
UL = Upper 95% confidence limit
PR = Protective Ratio (LD_{50}-treated/LD_{50}-untreated)
SE = Standard Error

Table 52

Summary of MREF Results with Mustard under Activity F.4

Mean lesion lengths in millimeters[a] from MREF Protocol 22, used to evaluate efficacies of Rohm and Haas candidate decontamination systems against HD at 1, 3 and 5 minutes.

Ambergard Resins	M258A1 I and II 1 min	3 min	5 min	Control	Candidate System 1 min	3 min	5 min
XE-555	24.7	27.4	29.2	33.2	19.6[c]	22.7[c]	24.7[c]
XE-556	21.6	22.3	24.2	32.0	19.7[c]	21.6[b]	23.5[c]

[a] The criterion for passing is that the contralateral differences (M258 less candidate) in mean lesion length are equivalent to or greater than zero for all time periods.
[b] Equivalent to the M258A1 standard decontamination system estimates at corresponding time periods.
[c] Significantly less ($P<0.05$) than the M258A1 standard decontamination system estimates at corresponding time periods.

Table 53

Summary of MREF Results with Lewisite under Activity F.4

Mean lesion lengths in millimeters[a] from MREF Protocol 22 used to evaluate efficacies of Rohm and Haas candidate decontamination systems against L at 30, 60, and 120 seconds.

Ambergard Resins	M258A1 I and II 30 s	60 s	120 s	Control	Candidate System 30 s	60 s	120 s
XE-555	16.4	16.1	16.5	23.2	16.4[b]	18.1[d]	19.4[d]
XE-556	16.8	17.3	17.3	23.1	16.3[b]	17.7[b]	19.2[d]

[a] The criterion for passing is that the contralateral differences (M258 less candidate) in mean lesion length are equivalent to or greater than zero for all time periods.
[b] Equivalent to the M258A1 standard decontamination system estimates at corresponding time periods.
[c] Significantly less ($P<0.05$) than the M258A1 standard decontamination system estimates at corresponding time periods.
[d] Significantly greater ($P<0.05$) than the M258A1 standard decontamination system estimates at corresponding time periods.

Two criteria for the evaluation of the data in the previous five tables must be considered. First, do the candidate resin systems provide the same level of protection as the M258A1 kit? Second, does one of the two systems show a significant advantage over the other?

As shown in Tables 49 and 50, the protective ratios against GD and thickened GD for the candidate systems are slightly better than for the M258A1 kit. The difference in protection between the resin systems and the M258A1 is not significant, nor is a significant difference seen between the two candidate systems.

The data in Table 52 show the candidate systems to be significantly better than the M258A1 at reducing mustard lesion lengths in five out of six test conditions. The two candidate systems were not directly compared to one another, and no significant advantage of one over the other is evident.

The data in Table 53 show the Ambergard XE-555 resin to be less effective than the M258A1 at reducing Lewisite lesion lengths. The Ambergard XE-556 resin performs approximately equally to the M258A1. While a statistically significant difference between the M258A1 and the candidate systems exists (and probably an advantage of Ambergard XE-556 resin over Ambergard XE-555 resin), a biologically significant difference is difficult to justify. In other words, as with M258A1, some efficacy is seen; however, a significant lesion is still evident. The observed differences are not considered great enough to justify selection of the Ambergard XE-556 resin over the Ambergard XE-555 resin.

The final data for consideration are the VX data in Table 51. Both candidate systems show a significant level of protection against VX, although both are significantly less effective than the M258A1 kit. The difference in protective ratio of Ambergard XE-555 resin over Ambergard XE-556 resin is significant enough to consider the Ambergard XE-555 resin a better candidate system. Based on the VX testing of this activity, a selection of Ambergard XE-555 resin over Ambergard XE-556 resin is recommended.

This page is intentionally blank.

G. RESIN PREPARATION (ACTIVITY E)

1. Pilot Plant Operations

Construction of the Ambersorb pilot plant, funded by US Army contract DAMD17-83-C-3071, was completed ahead of schedule, from February through April 1985. All equipment was installed and the preliminary electrical checkouts were completed during this time.

Sufficient quantities of raw materials were prepared to operate the pilot plant for 4.5 months (continuously) and to satisfy the grinding requirements of the program. Most of these materials were processed to acceptable quality product, verifying the plant's ability to provide raw materials for the pilot plant's needs.

Prior to the startup of the Ambersorb pilot plant, both equipment and process operating instructions were written. The pilot plant start-up began the week of May 20, 1985, and owing to a series of equipment-related problems continued through August 1985. Mechanical and design problems were encountered with every major piece of equipment purchased from the equipment vendor.

Mechanical problems continued to plague the 1986 manufacturing campaign. To deal with these problems, an extensive program of routine and emergency maintenance was developed. This allowed us to continue the manufacturing runs despite the equipment problems. We now have a more complete understanding of our system which will enable us to propose system modifications for routine production when that becomes necessary.

Originally, the contract called for the preparation of a minimum of 4000 lbs of Ambersorb XE-348F. This requirement was later reduced to 3600 lb. Actually, 4200 lb were produced, 3800 lb of which were acceptable.

2. Grinding/Blending Experience

In December 1985 the identification of candidate toll grinding companies was begun. In addition to FDA registration we believed these companies must have jet mills, since jet mills are usually required to achieve particle sizes in the 5-to-15-micron range. Four candidate companies were selected based on their equipment and toll production capabilities. Of the four, one was eliminated because of poor housekeeping and lack of FDA experience. Following internal safety, health and environmental approval, the initial trials were conducted at the remaining facilities -- Particle Size Technology, Fine Grinding Corp., and Wedco.

During previous jet milling trials, the Amberlite IRA-900C(OH) resins suffered loss of some of their OH capacity from reaction with carbon dioxide in the air. As a result, the possible use of nitrogen in the jet mills was investigated. All companies we contacted informed us that it was impossible to substitute nitrogen for air in their systems due to the huge volumes of compressed air used in grinding. Thus with a jet mill system, degradation of the Amberlite IRA-900C(OH) resin functionality is unavoidable. Another option to preserve Amberlite IRA-900C(OH) resin quality was to grind cryogenically. However, preliminary information indicated that cryogenic grinding is not generally capable of achieving particle size reduction down to the 5-micron size, and thus it was decided not to pursue this option under this contract.

At all three locations jet milling was a failure. Based on the preliminary grinding trials, we reached the following conclusions:

a. Jet milling is not a feasible option for grinding Amberlite IRA-900C(OH) resin, Amberlyst XN-1010(H) resin and Ambersorb XE-348F adsorbent to approximately 5 microns for the following reasons:

   (1) So much energy, and hence air pressure, is required to jet mill whole beads that product collection becomes a major problem. High material losses are inevitable.

   (2) At most, only about 70% of the feed material can be ground in one pass. Unground whole beads must be separated and re-fed, usually through an air classifier. This added air compounds the product recovery problem.

b. Mechanical milling can achieve particle size reduction down to our target range. Thus, mechanical milling is a feasible option as either a first pass prior to jet milling or perhaps even as a single processing step.

c. Jet milling Amberlite IRA-900C(OH) resins significantly reduces their OH functionality. This degradation is not seen in mechanical milling and is not as severe when the jet milling is preceded by mechanical milling. This is true, of course, only when large quantities of air are not used for product isolation and collection.

d. The most feasible equipment for grinding our materials is a mechanical mill in which residence time can be extended and which does not use air for classification.

In June 1986 we began to search for FDA-registered toll facilities with ball mills or equivalent equipment, since these mills would allow us to increase residence time to assure complete grinding. It was apparent from contacts with 22 companies that locating an FDA-approved toll facility that has

ball mills or equivalent equipment would be difficult. Ball mills are generally not used to grind to the particle size we require. As a result, many of the facilities with ball mills use them to coarse-grind minerals or other inorganics, and thus FDA materials cannot be run in their units. Most drug-manufacturing facilities have converted from ball mills to other mechanical mills such as air-classifying mills (ACMs), hammer mills, vertical mills, or Fitz mills. These are all continuous units capable of performing fine grinding of their materials, but there is little or no control over residence time. Most have air classifiers or use large volumes of air to recover product. They are not suitable for our application, since our materials are difficult to fracture and thus require extended residence times, and since recycle or product recovery with air drastically increases material losses through the filter bags.

Earlier, in January 1985, Pioneering Applications Research (PAR) personnel had run a trial at Sweco in Florence, KY, in their Vibro-Energy mill. This trial indicated that Ambersorb XE-348F could be ground to 10.2 microns in 1 hour, and to 4.8 microns in 4 hours. Because of this successful trial we contacted Sweco to determine whether any of their Vibro-Energy mill customers were in the toll grinding business. We were told that they knew of no toll grinding companies with these mills, since such units are generally purchased for specialized applications. However, rental units were available from Sweco.

We also learned that Union Process, in Akron, OH, reportedly processed foods and pharmaceutical products. They manufacture the "Attritor" mill, an internally agitated ball mill which can be run wet or dry, batch or continuous. They also toll grind materials, although they are more in the business of equipment sales. As a result, we decided to pursue two routes to provide materials for the prototype kits -- using a rented Sweco mill and conducting trials at Union Process. Approximately 100 lb of Ambergard XE-555 resin and 100 lb of Ambergard XE-556 resin were required for the prototype kits.

The Sweco mill arrived on July 30, 1986, and was set up in our Spring House facility. Operating procedures were written and a safety review conducted. Proper procedures were followed to assure the materials were produced in compliance with FDA Good Manufacturing Practices (GMP).

In all, 55 batches were run in the 1-cu-ft Sweco mill, producing sufficient materials for 181 lb of Ambergard XE-555 resin and 196 lb of Ambergard XE-556 resin. However, a number of processing problems were encountered with this unit. These problems included long cycle times and extended cool-down times, since the Sweco mill was not jacketed and thus had no means of removing the heat generated during grinding. As a result of these deficiencies, we concluded that the Sweco mill was not the best unit for our long-term needs. In addition, in view of the subsequent success of the Attritor-mill studies (below), these

materials were not used for the manufacture of the PCDS SDK prototypes.

During August 1986 we conducted preliminary tests at Union Process in their 1-gal Attritor mill. This is an internally agitated ball mill which can be used to achieve particle-size reduction to the micron level. The preliminary tests resulted in Amberlyst XN-1010(H) resin ground to a mean size of 7.8 microns and Ambersorb XE-348F adsorbent ground to a mean size of 10.3 microns. Initially Union Process could not grind Amberlite IRA-900C(OH) resin, since it clumped and caked because of its high moisture content. Union Process then blended the Amberlite IRA-900C(OH) resin with the previously ground Amberlyst XN-1010(H) resins and Ambersorb XE-348F adsorbents, based on the percentages required for the Ambergard XE-556 resin. The Amberlite IRA-900C(OH) resin became more free-flowing and Union Process successfully ground the material, achieving a final mean size of 5.5 microns. In a subsequent laboratory trial in their 1-gal unit, they successfully ground all three components together at once, with a resultant mean size of 8.4 microns. Although some heat was generated both in the blending and then in the grinding, the unit was jacketed and Union Process was quickly able to find an optimum cooling water rate to remove the heat.

Following a safety, health and environmental review of the Union Process facility we prepared a total of seven batches of Ambergard XE-555 resin and seven batches of Ambergard XE-556 resin The following materials were produced:

Ambergard XE-555 Resin	220 lb
	7.9 microns average mean size
Ambergard XE-556 Resin	251 lb
	7.5 microns average mean size

Mean particle sizes ranged from 6.7 to 8.8 microns for these materials. From these materials, 109 lb of Ambergard XE-555 resin and 146.5 lb of Ambergard XE-556 resin were shipped to PACO for manufacture of the PCDS SDK prototypes.

The Union Process Attritor mill appears to be ideally suited for our grinding and blending needs. All three components plus the silica excipient can be processed together, producing either Ambergard XE-555 or Ambergard XE-556 resin in one step. Thus the need for a subsequent blending operation is eliminated. The unit is jacketed so that the heat generated from the mixing of Amberlite IRA-900C(OH) resin and Amberlyst XN-1010(H) resins can be easily controlled. This jacketing also removes heat created from friction during grinding, eliminating any need for cool-down time between batches. The mill can be swept with nitrogen during processing, assuring that Amberlite IRA-900C(OH) resin quality is maintained.

Prior to these runs Rohm and Haas conducted a GMP audit of the Union Process facility and found that the facility was not FDA-registered. Their experience handling FDA materials was only on a lab scale, not on a toll production basis. However, we determined that, with proper precautions and documentation, we could in fact produce the materials under GMP for the PCDS SDK prototypes in the Union Process 30-gal unit. Based on this audit, we prepared operating instructions and batch cards to conform with Good Manufacturing Practices, and ran the trial strictly adhering to these procedures.

During November 1986 we completed the last phase of the grinding program, further grinding trials at Union Process, Akron, OH. During the GMP audit we had determined that any scale up beyond the 30-gal unit would not comply with GMP, since the large-scale equipment area could not be isolated or kept properly clean. Thus we decided not to run the large-scale trials originally planned, but instead to run an additional trial in the 30-gallon unit. This trial provided us with confirmation of cost data, and also provided additional process information and ground materials. We used the same system of equipment cleaning, batch records and other controls to adhere to Good Manufacturing Practices. We produced a total of 6 batches each of Ambergard XE-555 and XE-556 resins during this trial. We also conducted 1-gal trials to further study the grinding and blending process. All materials produced were in the acceptable mean particle size range, and all batches demonstrated a high degree of reproducibility (mean sizes 6 to 9 microns, standard deviation 0.7 microns, as measured by a Leeds and Northrup Microtrac particle-size analyzer.)

3. Dust Explosion Testing

Ambergard resins are powders with mean particle sizes in the 5- to 20-micron range. Since materials in this particle size range can pose explosion hazards, and since we must grind and handle these materials as part of our routine Ambergard resin production and end-use, we needed to evaluate their explosion potentials. All explosion testing was conducted by Fenwal, Inc., Ashland, MA. Fenwal conducts initial "go/no go" testing at ambient and elevated temperatures first to determine whether or not a material is potentially explosive. If a material tests positive, Fenwal then conducts a series of tests to quantify and rank the explosion potential. These subsequent tests include such items as minimum explosive concentration, ignition energy, minimum ignition temperature, minimum oxygen concentration, and determination of a K_{st} value.

During the evaluation of jet milling, we submitted samples of the individual ground component resins to Fenwal for initial testing. Individual components were submitted because we were planning to grind the components separately, then blend them together to prepare the Ambergard resin. Explosion testing was

very important when jet milling was being considered, since there was a great potential for creating dust clouds with jet mills and air classifiers. The preliminary tests indicated that the ground Amberlyst XN-1010(H) resins and Amberlite IRA-900C(OH) resins were both potential dust explosion hazards, while the ground Ambersorb XE-348F adsorbent was not. No further work was done with the individual components, however, owing to the change in grinding equipment from jet mills to the Attritor mill.

Following the successful trials at Union Process, we again submitted samples to Fenwal for their preliminary testing. This time, however, we submitted samples of Ambergard XE-555 and XE-556 resin, since we were no longer planning to process the individual components. In the Union Process trials we had noted that the materials dusted much less, because of the higher moisture levels resulting from the new process. This process also eliminated a source of dusting during processing, since materials were now processed in a closed system without large volumes of air. The preliminary tests indicated that, at ambient temperatures, the Ambergard XE-555/556 resin posed no explosion hazard. Only at very elevated temperatures (in a furnace at 1400°F) did the materials exhibit any evidence of a flame. As a result of these tests, we concluded that further testing was not necessary under the current contract, since the materials posed no explosion danger under normal processing or end-use conditions.

4. Additional Grinding Studies

During the kit preparation phase, we had found that materials produced at Union Process in the Attritor mill (the preferred grinding and blending system) had a higher moisture content than the previously prepared materials. Because of this higher moisture level, PACO experienced difficulty in kit preparation, which resulted in longer fill times. Thus we planned to set up a one-gallon Model 1-SDG Attritor mill in the building housing the Pilot Plant, and prepare Ambergard XE-555/556 resins under various conditions to study the effect on moisture content. These samples could then be tested for flowability, and some measure of the ease of packaging determined.

Before this program could be initiated, we became aware of the potential dusting problem encountered during the user tests of the kits. As a result, we shifted the emphasis of this study to address immediately the dusting issue. We decided to prepare materials with various grind times (and thus various particle sizes) and study the effect of particle size on dusting. We decided to conduct the study in a small laboratory mill. The laboratory mill is less desirable than the Attritor mill because of the lack of confidence in the scalability of particle size distributions with lab grinders.

Table 54 summarizes the mean particle size, X90 (the size below which 90% of the material falls) and percent moistures for materials ground from 1 to 20 min. The X90 data are a measure of how much large-sized material is present. In addition, representative data of materials prepared with the Attritor mill are included for reference. Although the effect of moisture content was not examined in this study, the data are presented to verify that the moisture content was held constant, equal to that of the Attritor mill materials.

Table 54

Summary of Grinding Data - Ambergard XE-555 Resin Ground in Laboratory Mill

Time (min)	Mean Size (microns)	X90 (microns)	Moisture Content (%)
1	24.2	96.7	-
3	21.5	95.0	29.4
5	19.3	90.9	30.7
10	12.3	85.1	29.7
15	11.9	80.9	29.3
20	10.4	78.1	29.2
Attritor	10.0	33.0	29.0

The materials ground by the Union Process Attritor mill result in powders with a much narrower particle-size distribution. Assuming this "sharpness" in the particle-size distribution can be maintained while the mean particle size of the powder is increased, the prospect of reducing the respirable fraction in the sample is enhanced.

This page is intentionally blank.

H. SPECIFICATIONS

Samples of raw materials for the Ambersorb resins were pyrolyzed at a range of temperatures in the laboratory in order to evaluate our characterization tests. Based on these results and on the pilot plant manufacturing experience, preliminary in-process control tests and final product specifications which had been established for Ambersorb XE-348F adsorbent prior to this contract were found to be acceptable for the Ambergard resins. In addition, we set initial specifications for Ambergard XE-555 and XE-556 resins, as well as for all raw materials used for these products (Amberlyst XN-1010(H) resin and Amberlite IRA-900C(OH) resin). These preliminary specifications are summarized in Tables 55 and 56.

Table 55

Preliminary Specifications for Reactive Resins Used in Ambergard Resins

Amberlite IRA-900C(OH) resin:	
Equivalent OH (%)	80, minimum
Exchange Capacity, Wt (dry, meq/g)	3.7, minimum
Appearance	FFVFM[a]
Moisture (%)	Report value (expect 66 - 73)
Amberlyst XN-1010(H) resin:	
Exchange Capacity, Wt (dry, meq/g)	3.0, minimum
Surface Area (m^2/g)	Report value (expect >400)
Appearance	FFVFM[a]
Solids (%)	Report value (expect >95)

[a] FFVFM = Free from visible foreign matter

Table 56

Preliminary Specifications for Ambergard XE-555 and XE-556 Resins

	Ambergard XE-555 Resin	Ambergard XE-556 Resin
Mean Particle Size (microns)	5-20	5-20
Acidity (meq/g)	Report value (expect 0.67 minimum)	Report value (expect 0.32 minimum)
Basicity (meq/g)	Report value (expect 0.59 minimum)	Report value (expect 0.78 minimum)
Moisture (%)	Report value (expect 27-31)	Report value (expect 34-38)
Appearance	FFVFM[a]	FFVFM
Basicity/Acidity	0.8 - 1.2	1.8 - 2.2

[a] FFVFM = Free from visible foreign matter.

Note that these specifications are preliminary, based on our best experience to date. Further laboratory studies will be required to better define these specifications prior to any routine Ambergard XE-555 and XE-556 resin production. For instance, some additional end-use application specification, such as vapor desorption analysis, may be desirable. This should be studied further in subsequent programs.

All the Amberlyst XN-1010(H) resin used for this program came from only two batches; as a result, the specifications for this material are quite tentative. Also, the moisture content of Amberlite IRA-900C(OH) resin appears to vary considerably from batch to batch and even within a batch. This moisture affects the moisture level of the Ambergard resins, and thus has an effect on packaging efficiency at PACO. The effect of Amberlite IRA-900C(OH) resin and/or Ambergard XE-555 resin and Ambergard XE-556 resin moisture content on packaging efficiency should be studied also under some future contract, to allow us to set a moisture acceptance range.

Finally, we currently calculate the relative amounts of Amberlyst XN-1010(H) resins and Amberlite IRA-900C(OH) resins for the Ambergard resins based on the analysis of the acidity and

basicity of each lot of resins. Future work should examine whether this procedure is required for each lot of raw materials, or whether the percentages of resins could be fixed once more well-defined specifications are set for the resins.

This page is intentionally blank.

I. TRADE-OFF ANALYSIS

While the trade-off analysis was provided for inclusion in the data package for the Milestone I/II In-Process Review (IPR), this document is believed to provide a good overall summary for evaluation of the program accomplishments. The trade-off analysis is included in this report in its entirety with some minor changes in the original version reflecting the most recent results.

Below is a summary of the trade-offs of the PCDS SDK vs. the M258A1 followed by a brief explanation for each item. Most of the following information is a summary of data reported earlier in this report. The toxicity data for the M258A1 kit and kit components are from References 8 through 10.

1. Trade-Off Analysis Summary for PCDS SDK

Notation

>>>	Much Better Than
>	Better Than
=	Equal To
<	Worse Than
<<<	Much Worse Than
?>	Presumed Better Than
?=	Presumed Equal To
?<	Presumed Worse Than
?	Insufficient Data for Comparison

a. Safety

(1)	Acute Oral Toxicity	PCDS SDK	>>>	M258A1
(2)	Acute Dermal Toxicity	PCDS SDK	>>>	M258A1
(3)	Skin Irritation	PCDS SDK	>>>	M258A1
(4)	Eye Irritation	PCDS SDK	>>>	M258A1
(5)	Mutagenicity Tests (Ames)	PCDS SDK	?>	M258A1
(6)	Repeat Dermal Studies	PCDS SDK	>>>	M258A1
(7)	Delayed Contact Hypersensitivity	PCDS SDK	>>>	M258A1
(8)	Repeated Insult Patch Test (Humans)	PCDS SDK	>>>	M258A1
(9)	Reproduction Studies (Rats)	PCDS SDK	?>	M258A1
(10)	Inhalation Toxicity	PCDS SDK	?	M258A1
(11)	Reuse on Skin	PCDS SDK	>>>	M258A1
(12)	Materials of Kit Construction	PCDS SDK	>>>	M258A1
	OVERALL SAFETY.....	PCDS SDK	>>>	M258A1

b. Efficacy

(1)	In Vivo GD	PCDS SDK	=	M258A1
(2)	In Vivo TGD	PCDS SDK	=	M258A1
(3)	In Vivo HD	PCDS SDK	=	M258A1
(4)	In Vivo VX	PCDS SDK	<	M258A1
(5)	In Vivo L	PCDS SDK	=	M258A1
(6)	In Vivo T-2 Toxin	PCDS SDK	?=	M258A1
(7)	Vulnerability of Skin Following Decontaminant Exposure	PCDS SDK	?>	M258A1
	OVERALL EFFICACY.....	PCDS SDK	=	M258A1

c. Operational Factors

(1)	Area Coverage	PCDS SDK	>	M258A1
(2)	Decontaminations per Kit	PCDS SDK	>>>	M258A1
(3)	Stability	PCDS SDK	?>	M258A1
(4)	Not Degrade BDO/Mask	PCDS SDK	>	M258A1
(5)	Storage in Cold Climate	PCDS SDK	>	M258A1
(6)	Storage in Hot Climate	PCDS SDK	?>	M258A1
(7)	Kit Weight/Volume	PCDS SDK	>	M258A1
(8)	Battlefield Camouflage	PCDS SDK	=	M258A1
(9)	Compatible with Decon Detection Methods	PCDS SDK	>	M258A1
(10)	Transportability	PCDS SDK	>	M258A1
(11)	Supplemental Use - Decon of Uniform	PCDS SDK	?>	M258A1
(12)	Supplemental Use - Decon of Equipment	PCDS SDK	=	M258A1
(13)	Use of Kit for Training - Logistics	PCDS SDK	>>>	M258A1
	OVERALL OPERATIONAL FACTORS..	PCDS SDK	>	M258A1

d. Human Factors

(1)	Ease of Opening	PCDS SDK	>	M258A1
(2)	Ease of Use (1 vs. 2)	PCDS SDK	>>>	M258A1
(3)	Convenient to Carry	PCDS SDK	>	M258A1
(4)	Time of Decon	PCDS SDK	>	M258A1
(5)	Use in Cold Climate	PCDS SDK	>	M258A1
(6)	Use in Hot Climate	PCDS SDK	=	M258A1
(7)	Use in Contaminated Environment	PCDS SDK	=	M258A1
(8)	Use in Limited Visibility	PCDS SDK	>	M258A1
(9)	Training	PCDS SDK	>>>	M258A1
(10)	User Acceptance	PCDS SDK	?>	M258A1
(11)	Visual Indication of Decontamination	PCDS SDK	>>>	M258A1
	OVERALL HUMAN FACTORS.....	PCDS SDK	>	M258A1

e. Other

(1)	Cost per Decontamination	PCDS SDK	>	M258A1
(2)	Demilitarization	PCDS SDK	?>	M258A1
(3)	Amenable to Preplanned Product Improvement	PCDS SDK	>	M258A1

2. Basis for Trade-off Analysis Ratings

a. Safety

(1) Acute Oral Toxicity PCDS SDK >>> M258A1

In toxicity testing on both the component resins and the final formulations, the resins were determined to be practically non-toxic to male and female rats following a single oral administration (LD_{50} > 5000 mg/kg). In contrast, the M258A1 contents include phenol and sodium hydroxide. Phenol is classified as a DOT Poison B, with a reported oral LD_{50} of 414 mg/kg in rats. Sodium hydroxide is highly corrosive to all mucous membranes.

(2) Acute Dermal Toxicity PCDS SDK >>> M258A1

In toxicity testing on both the component resins and the final formulations, the decon resins were determined to be practically non-toxic to male and female rabbits following a single dermal dose (LD_{50} > 5000 mg/kg). In contrast, the M258A1 contents include phenol and sodium hydroxide. Phenol is classified as a DOT Poison B, with a reported SKN (systemic skin effects) LD_{50} of 850 mg/kg in rabbits. Sodium hydroxide is highly corrosive to all mucous membranes.

(3) Skin Irritation PCDS SDK >>> M258A1

In toxicity testing on both the component resins and the final formulations, the decon resins were determined to be slightly irritating and practically non-irritating to the skin of rabbits, respectively (72-hour Mean Irritation Scores were 0.5 and 0.0). In contrast, both components Decon 1 and Decon 2 of the M258A1, when applied separately and together caused severe irritation after 24 h. At concentrations that would be expected in actual usage, the components could still be classified as moderate irritants. Sodium hydroxide is classified as a DOT corrosive and is reported to have severe skin irritation effects on rabbits at 50 mg/2 h.

(4) Eye Irritation PCDS SDK >>> M258A1

In toxicity testing on both the component resins and the final formulations, the decon resins were determined to be inconsequentially irritating to the eyes of rabbits (all ocular effects were reversible within 24 h). In contrast, the M258A1 contents include phenol and sodium hydroxide. Phenol is reported to have severe eye irritation effects on rabbits at 5 mg sodium hydroxide is classified as a DOT corrosive and is reported to have severe eye irritation effects on rabbits at 0.050 mg.

(5) Mutagenicity Tests (Ames) PCDS SDK ?> M258A1

The decon resins did not demonstrate mutagenic activity. The resins were negative (no effect) in the Microbial Mutagen (Ames) test. In contrast, the M258A1 contains phenol. Phenol is reported to be an experimental mutagen and carcinogen.

(6) Repeat Dermal Studies PCDS SDK >>> M258A1

The decon resins were determined, as a result of repeated dermal exposure, to be practically non-toxic to male and female rabbits, but to be slightly irritating to intact and abraded skin (5.0 g/kg/day for 10 days). In contrast, the M258A1 contents include phenol and sodium hydroxide. Phenol is classified as a DOT Poison B, with a reported SKN (systemic skin effects) LD_{50} of 850 mg/kg in rabbits, and is reported to have severe skin irritation effects on rabbits at 500 mg/24 h. Sodium hydroxide is classified as a DOT corrosive and is reported to have severe skin irritation effects on rabbits at 50 mg/24 h.

(7) Delayed Contact Hypersensitivity PCDS SDK >>> M258A1

The decon resins were determined to not produce delayed contact hypersensitivity in guinea pigs. In contrast, the M258A1 components are severely irritating to the skin as noted above.

(8) Repeated Insult Patch Test (Humans) PCDS SDK >>> M258A1

The component resins and the final formulations were evaluated in a repeated insult patch test designed to determine human skin sensitization potential of the materials. No evidence of delayed contact hypersensitivity was observed with the decon resins in humans. In contrast, the M258A1 components are severely irritating to the skin as noted above.

(9) Reproduction Studies (Rats) PCDS SDK ?> M258A1

A 13-week one-generation dermal exposure with the decon resins was conducted to evaluate potential cumulative toxicity and reproductive effects. No treatment-related signs of toxicity were observed in male rats following 13 weeks of dermal treatment (500 mg/kg) with XE-551. No adverse effects were detected for any adult reproductive parameter after exposure to XE-551. No treatment-related effects were noted on pup survival or pup body weight. In contrast, the M258A1 contains phenol. Phenol is reported to be an experimental mutagen and carcinogen.

(10) Inhalation Toxicity PCDS SDK ? M258A1

Sub-acute inhalation findings (rats) on the decon resins were typical of findings for material exceeding the capacity of the lungs. Histopathologic examination of the lungs showed accumulations of macrophages containing black particles in the areas of the terminal bronchioles and the alveolar ducts at respirable concentrations of 7 mg/m^3 and higher. Using the presence of inflammation as the minimum criterion for an adverse effect, the lowest-observed-adverse-effect level (LOAEL) was 320 mg/m^3, based on total concentration, and 117 mg/m^3 based on respirable concentration. The no-observed-adverse-effect level (NOAEL) for 2 weeks of nose-only inhalation exposure to Resin XE-519 was 13 mg/m^3, based on total concentration, and 7 mg/m^3, based on respirable concentration. After 4 weeks of post-exposure recovery, the NOAEL was unchanged.

(11) Reuse on Skin PCDS SDK >>> M258A1

The PCDS SDK does not have a significant detrimental effect on skin integrity. In contrast, as noted above, the M258A1 components are severely corrosive to skin. The resulting skin damage would be expected to result in a significantly faster agent penetration of the skin. Similarly, the detrimental effects of the M258A1 would be compounded upon repeated applications.

(12) Materials of Kit Construction PCDS SDK >>> M258A1

The PCDS SDK contains no potentially hazardous materials of construction. In contrast, the M258A1 Decon 2 contains a glass ampoule which must be crushed to release the chloramine-B. The potential exists for glass particles to be entrapped in the towelette, and as a result cut the skin.

b. Efficacy

(1) In Vivo GD PCDS SDK = M258A1

Protective ratio tests against GD with the final resin formulations are in progress at Battelle-MREF. Preliminary results indicate that the PCDS SDK has a level of efficacy approximately equivalent to the protection provided by the M258A1 kit against GD under the test conditions.

(2) In Vivo TGD PCDS SDK = M258A1

The PCDS SDK resin components were evaluated on rabbits in a screening test against M258A1 following TGD exposure. The powder resin systems were determined to be statistically as good as or better than the standard M258A1 decontamination. Protective ratio tests against TGD with the final resin formulations is in progress at Battelle-MREF.

Preliminary results indicate that the PCDS SDK has a level of efficacy approximately equivalent to the protection provided by the M258A1 kit against TGD under the test conditions.

(3) In Vivo HD PCDS SDK = M258A1

The PCDS SDK resin components were evaluated on rabbits in a screening test against M258A1 following HD exposure. The powder resin systems were determined to be statistically as good as or better than the standard M258A1 decontamination. Definitive efficacy testing with the final resin formulations is in progress at Battelle-MREF. Preliminary results indicate that the PCDS SDK has a level of efficacy approximately equivalent to the protection provided by the M258A1 kit against HD under the test conditions.

(4) In Vivo VX PCDS SDK < M258A1

The PCDS SDK resin components were evaluated on rabbits in a screening test against M258A1 following VX exposure. The powder resin systems were determined to be statistically less effective than the standard M258A1 decontamination. Protective ratio tests against VX with the final resin formulations are in progress at Battelle MREF. Preliminary results indicate that the PCDS-SDK provides protection against VX, but is not as effective as the M258A1 kit under the test conditions.

(5) In Vivo L PCDS SDK = M258A1

Definitive efficacy testing with the final resin formulations following L exposure is in progress at Battelle MREF. Preliminary results indicate that the PCDS SDK has a level of efficacy approximately equivalent to the protection provided by the M258A1 kit against L under the test conditions.

(6) In Vivo T-2 Toxin PCDS SDK ? M258A1

Initial screening tests with the final resin formulations following T-2 mycotoxin exposure are in progress at USAMRIID. Preliminary results indicate that the PCDS SDK provides some efficacy against T-2 under the test conditions. The M258A1 kit is reported in USAMRIID's testing protocol as being effective in removing T-2 mycotoxin from the skin of the rat, but the toxin was not neutralized or chemically degraded. Thus, the scrubbing action deployed in the use of the M258A1 kit was responsible for removal of T-2 mycotoxin from the skin of the rat. A similar physical removal may be expected from the PCDS SDK.

(7) Vulnerability of Skin Following Decontaminant Exposure — PCDS SDK ?> M258A1

The PCDS SDK does not have a significant detrimental effect on skin integrity. No increase in vulnerability would be expected following skin exposure to the resin systems, whether as result of a prior chemical attack or as a result of a false alarm. In contrast, the M258A1 components are severely corrosive to skin and would presumably result in a significantly faster agent penetration of the skin following a prior decontamination procedure, whether real or mistaken.

c. Operational Factors

(1) Area Coverage — PCDS SDK > M258A1

PCDS SDK individual packet area coverage data, generated using rough Kydex plastic surfaces and thickened methyl salicylate (TMS) as a simulant, meet or exceed the JSOR area coverage requirement of 1300 cm^2 at a challenge level of 2.5 g/m^2 agent (simulant). (See separate section on area coverage.) Additionally, in vivo data conducted at Battelle-MREF can be extrapolated to support the in vitro area coverage data. At a threat concentration of 2.5 g/m^2 TGD, one packet (2.8 g) should decontaminate at least an 840 to 1680 cm^2 area. In contrast, to our knowledge, no experimental data exists for the area coverage of the M258A1 kit.

(2) Decontaminations per Kit — PCDS SDK >>> M258A1

The PCDS SDK contains six packets, and therefore will provide for up to six decontaminations based on the 1300 cm^2 area coverage requirement specified in the JSOR. In contrast, the M258A1 contains only three packets of each component, and therefore will provide for only up to three decontaminations.

(3) Stability — PCDS SDK ?> M258A1

Long-term storage stability and shelf-life determinations are in progress and actual values have not yet been established for the PCDS SDK. The efficacy of the resin system is primarily attributed to the rapid removal of agents from the skin surface (sorption). Destruction of the agents is an important secondary process. No decomposition of the sorptive resins under very long storage conditions would be expected. Some thermal decomposition of the reactive resin will occur with time, but a corresponding loss of efficacy may not occur. Accelerated stability testing of the component resins still show significant reactivity after 1 year's storage at temperatures up to 60°C (140°F). (See separate section on resin stability testing.)

(4) Non-degradation of BDO/Mask PCDS SDK > M258A1

The PCDS SDK is not expected to degrade the BDO or mask. Initial tests with simulants show no degradation of the BDO material. Tests with the mask are planned. No adverse effects are expected based on the non-corrosivity of the resin systems. In contrast, the highly corrosive nature of the M258A1 may have some detrimental effects on uniform fabrics.

(5) Storage in Cold Climate PCDS SDK > M258A1

The PCDS SDK can be stored in cold and extreme cold climates. The powdered resins remain free flowing under extremely cold conditions; no liquid components exist to freeze. Fabrication materials (packaging) will be designed to withstand extremely cold environments. In contrast, the M258A1 may freeze under extremely cold conditions. Thawing would be necessary prior to use.

(6) Storage in Hot Climate PCDS SDK ?> M258A1

While the long-term shelf life for the PCDS SDK has not been established yet, no change in the sorptive properties is expected. Some degradation of the reactive resin will occur at elevated temperatures. Fabrication materials (packaging) will be designed to withstand hot environments. In contrast, the M258A1 is not to be stored above 110°F.

(7) Kit Weight/Volume PCDS SDK > M258A1

The weight of the advance development PCDS SDK prototype (approximately 40 grams for 6 packets in a soft-pack case) is about 1/3 of the weight of the M258A1 decon kit (approximately 130 g for three each Decon 1 and Decon 2 in a hard case). The volume of the PCDS SDK prototype is approximately equal to the volume of the M258A1 kit.

(8) Battlefield Camouflage PCDS SDK = M258A1

The PCDS SDK packets and soft pack are colored olive drab, as are the packets and hard pack for the M258A1 kit.

(9) Compatible with Decon Detection Methods PCDS SDK > M258A1

The PCDS SDK does not cause any response on M-8 chemical agent detection paper. Although not yet demonstrated, no false alarms are expected with alarm systems (CAM). In contrast, the M258A1 components Decon 1 and Decon 2 both cause color changes on M-8 paper that may be confused with VX and G agent responses, respectively.

(10) Transportability PCDS SDK > M258A1

The PCDS SDK contains no flammable or breakable components. In contrast, the M258A1 contains alcohol. The alcohol content may result in restrictions on air shipments.

(11) Supplemental Use - Decon of Uniform PCDS SDK ?> M258A1

While not yet demonstrated, it is expected that the PCDS SDK can be used for uniform (fabric) decontamination. In contrast, current doctrine prohibits use of the M258A1 for decontamination of the uniform. Because of this, the Army is currently investigating alternatives for material decon.

(12) Supplemental Use - Decon of Equipment PCDS SDK = M258A1

While not yet demonstrated, it is expected that the PCDS SDK can be used for personal equipment decontamination. The M258A1 kit is also acceptable for this use.

(13) Use of Kit for Training/Logistics PCDS SDK >>> M258A1

The PCDS SDK can be used both for actual field use and for training purposes. In contrast, the M258A1 cannot be used for training purposes owing to the highly corrosive nature of the kit. As a result of this, a separate placebo kit must be procured, stored, and distributed for training purposes.

d. Human Factors

(1) Ease of Opening PCDS SDK > M258A1

The opening of the PCDS SDK requires only that the flaps be peeled apart. The flaps were designed to be large enough to be used with the bulky protective gloves; this procedure was validated during user testing. In contrast, the M258A1 requires opening the hard case, removing the proper packet, tearing open the packet, and removing and unfolding the towelette. Some difficulty with these manipulations may be experienced when wearing gloves.

(2) Ease of Use (1 vs. 2) PCDS SDK >>> M258A1

The use of the PCDS SDK requires only that the packet be peeled open and rubbed on the skin. The PCDS SDK is a one-component system. In contrast, the M258A1 contains two components that must be used in the proper sequence. Decon 2 requires that a glass ampoule be crushed and separated from the towelette.

(3) Convenience in Carrying PCDS SDK > M258A1

The PCDS SDK has no sharp or breakable materials of construction. Therefore, it was possible to fabricate a soft pack for the carrying container. This soft pack can be easily carried in the thigh pocket of the BDU/BDO. In contrast, the M258A1 Decon 2 contains a glass ampoule which must be protected from breakage. A hard case was therefore necessary for the carrying container.

(4) Time of Decon PCDS SDK > M258A1

The PCDS SDK is a one-component, easily opened packet. The instructions say to rub exposed skin for 2 to 3 min. In contrast, the M258A1 is a two-component system requiring some manipulation prior to use of each component. The instructions say to rub Decon 1 for 1 min and Decon 2 for 2 to 3 min.

(5) Use in Cold Climate PCDS SDK > M258A1

The PCDS SDK remains a free-flowing powder at low temperatures. No difficulties in using the kit at low temperatures are anticipated. In contrast, the training manual for the M258A1 kit specifies the normal operating temperature as being above 32°F, although use below 32°F is acceptable as long as the wipes in the packets are not frozen.

(6) Use in Hot Climate PCDS SDK = M258A1

The PCDS SDK is suitable for use in any hot environment expected to be encountered. Similarly, the normal operating temperature for the M258A1 is up to 110°F.

(7) Use in Contaminated Environment PCDS SDK = M258A1

The PCDS SDK contains individually packaged applications. Each packet's contents remain protected from contamination prior to opening. Similarly, the M258A1 kit contains individually packaged applications.

(8) Use in Limited Visibility PCDS SDK > M258A1

The PCDS SDK is easily opened and used. As only one component is necessary, selection of the proper packet under reduced visibility is not an issue. In contrast, the M258A1 requires selection of Decon 1 packets first. Tabs are used to aid in identification of the packets. Decon 2 requires that the mesh containing the broken glass ampoule be removed. These manipulations may be more difficult under conditions of reduced visibility.

(9) Training PCDS SDK >>> M258A1

The PCDS SDK is a one-component, simple to use system which is also acceptable for training purposes. The simplicity of use of the PCDS SDK should also simplify training. In contrast, the M258A1 kit is a two-component, multiple-step system, which cannot be used for training purposes. A placebo kit is used for training, with the result that the user never gains experience with the M258A1 kit prior to the necessity for actual field use.

(10) User Acceptance PCDS SDK ?> M258A1

The PCDS SDK has undergone limited user tests at Ft. Knox (application) and Ft. Bragg (durability). The final report is not yet available. However, initial indications are that the prototype kits were generally well accepted. In contrast, the M258A1 kit cannot be used for training.

(11) Visual Indication of Decontamination PCDS SDK >>> M258A1

The PCDS SDK is a black powder. A visual indication of skin surfaces having been decontaminated is immediately evident because of the remaining powder. In contrast, the M258A1 kit contains clear solutions. No similar indication of treated skin surface is present.

e. Other

(1) Cost per Decontamination PCDS SDK > M258A1

The PCDS SDK cost per kit will be a function of the final production/fabrication method. It is estimated that the final kit will cost less than the M258A1 kit when compared on a per decontamination basis.

(2) Demilitarization PCDS SDK ?> M258A1

The PCDS SDK contents are non-hazardous materials. Landfill will likely be an acceptable disposal method for these kits. In contrast, the M258A1 kit contains toxic and corrosive materials. Special disposal techniques may be necessary for these materials.

(3) Amenable to Preplanned Product Improvement PCDS SDK > M258A1

The PCDS SDK system contains ground reactive and sorptive resins. When new, improved resins, currently under development, are identified, they can easily be incorporated into the existing packaging systems.

This page is intentionally blank.

J. FDA ISSUES

A draft copy of the petition for exemption for an investigational new drug (IND) intended for submission to the FDA was submitted to USAMRDC for approval in July 1985. After revision, the petition was approved by the Human Use Review Board and submitted to the FDA in October 1985 (IND No. 27,295). The petition was a joint submission from Rohm and Haas Company and the U.S. Army Medical Materiel Development Activity for human safety testing (skin irritation) and not for any efficacy studies. The submission covered only the initial laboratory-scale preparation of material for a small amount of testing. It defined the individual unground resins as bulk raw materials so that there should be no question of FDA regulation of their manufacture. An attempt was made in the submission to define the start of drug manufacture at the grinding/mixing operation.

Repeat, human dermal irritation studies on the unformulated decon resins were initiated at Hill Top Laboratories in January 1986. No evidence of delayed contact sensitization was observed with any of the materials. Results of the testing (summarized in Section D of this report) were submitted to the FDA on April 30, 1986.

As this project progressed, it became evident that the restrictions for handling, labeling and use that are attendant to an investigational drug were burdensome and probably unnecessary for the materials under development. Thus, in June 1986 a petition was submitted to the FDA in the form of letters from the Rohm and Haas Co., USAMMDA , and the U.S. Army Chemical School. This petition requested release from the drug classification for skin decontaminants. The request was based on a number of arguments, including the FDA's legal definition of a drug and the safety and efficacy assurance that the Army will provide for any fielded material.

In September 1986, an amendment to the original IND was submitted to the FDA for permission to carry out additional human dermal irritation studies on the final formulated Ambergard XE-555 and Ambergard XE-556 resins. Our request for re-classification was still pending and this amendment was necessary to continue the progress of the contract. On October 14, the FDA officially responded to the reclassification petition and agreed that the Ambergard resins were no longer considered drugs for Department of Defense chemical agent removal applications. Subsequently, the original IND submission and its amendment were discontinued. By the time the final PCDS SDK prototypes were fabricated, the materials were no longer considered drugs.

This page is intentionally blank.

K. CONCLUSIONS AND RECOMMENDATIONS

1. Conclusions

a. Based on the in vitro evaluations of the initial six candidate resin systems, XE-519 and XE-521 are the most efficacious resins.

b. Based on further in vitro and in vivo evaluations of formulated resin systems, powdered systems are the only viable formulation. Efficacy is maximized when excipient levels are kept to the minimum required to yield the desired physical characteristics. Ambergard XE-555 and Ambergard XE-556 resins have the best overall characteristics.

c. Based on the final definitive in vivo efficacy testing, Ambergard XE-555 and Ambergard XE-556 resins provide protection against GD, TGD, HD, and L at a level equivalent to the M258A1 kit.

d. Based on the VX portion of the final definitive in vivo efficacy testing, Ambergard XE-555 resin is more effective than Ambergard XE-556 resin against VX (protective ratio 22.8 vs. 16.6), but less effective than the M258A1 (PR = 43.2). Therefore, Ambergard XE-555 resin is considered to be the best candidate for moving into full scale development.

e. Based on all the toxicological findings, formulated and unformulated candidate decontamination resins are very safe for use in a personal skin decontamination system.

f. Based on in vitro agent testing with GD, HD, and VX conducted by Midwest Research Institute, the formulation excipients do not have an adverse effect on resin performance; and the trends seen with simulant testing hold with agents, although the resins are more reactive toward agents than simulants.

g. Based on the limited accelerated stability testing, the candidate resin systems retain an unexpectedly high degree of their reactive and sorptive capabilities. Better evaluation methods will need to be developed before a shelf life can be determined, but the initial results are encouraging.

h. Based on evaluation of delivery system concepts, the best delivery system is a single dose resin impregnated fiberfill pad, which acts both to apply and to remove the resin.

i. Based on area coverage data generated under controlled laboratory conditions, one SDK packet may decontaminate in excess of 1300 cm^2 of surface area. Doctrinal considerations and field use conditions will need to be evaluated prior to the establishment of final use instructions.

j. Based on carbonaceous resin preparation efforts, the Ambersorb adsorbent pilot plant is capable of producing 1000-lb quantities of Ambersorb XE-348F adsorbent. However, it can meet long-term production demands only following further equipment upgrades and a detailed process study.

k. Based on evaluation of various grinding processes, the Attritor mill, manufactured by Union Process, is ideally suited for grinding and blending the materials used in production of the Ambergard resin.

l. Overall, the prototype PCDS SDK offers numerous advantages over the currently-fielded M258A1 kit, as outlined in the trade-off analysis.

2. Recommendations

It is recommended that:

a. the program be transitioned to full-scale development;

b. Ambergard XE-555 resin be selected as the decontaminant of choice in the full-scale-development phase, based on in vivo protective ratio results;

c. the pilot plant equipment be upgraded to permit more streamline operation and a process study be initiated concurrently with full-scale development; d. intermediate and final product specifications be examined further during full-scale development.

REFERENCES

1. "Annual Report, Development of a Safe and Effective Skin Decontamination System"; Rohm and Haas Company; USAMRDC contract DAMD17-85-C-5200; 30 September 1986.

2. "A Selective Review and Assessment of Potential Application of Ion-Exchange Resins in Chemical Analysis, Protection, and Detoxification"; G.E. Janauer; Chemical Systems Laboratory; Report No. ARCSL-SP-81023; January 1983 (Unclassified, AD-B071 520).

3. "Sorbent Powders for Chemical Warfare Decontamination"; T.B. Stanford; ASD-TR-82-5010; April 1982 (Unclassified, AD-B064 597L).

4. "Some Considerations for Choosing Decontamination Simulants"; D. Long, V. Wallace; Chemical Laboratory Division, U.S. Army, Dugway Proving Ground, Dugway, Utah; September 1981 (Unclassified, AD-B063 326).

5. "Thermal Decomposition of Amberlite IRA-400"; E.W. Baumann; J. Chem. Eng. Data; Vol. 5; 376-382; 1960.

6. "Laboratory Methods for Evaluating Protective Clothing Systems Against Chemical Agents"; CRDC-SP-84818; June 1984 (Unclassified, AD-B084 711L).

7. See for example: "Percutaneous Absorption in Man and Animal: A Perspective"; R.C. Webster, H.I. Maibach; in Cutaneous Toxicity; V.A. Drill, P. Lazar, eds.; Academic Press; New York; 1977; pp. 111-126.

8. "Primary Dermal Irritation Potential of Components of the M258A1 Decontamination Kit (Study 1)"; J.T. Fruin, M.A. Haynes; Letterman Army Institute of Research; Report No. 101; September 1981 (Unclassified, AD-A105 977).

9. "Primary Dermal Irritation Potential of Components of the M258A1 Decontamination Kit"; J.T. Fruin, M.A. Haynes; Letterman Army Institute of Research; Report No. 120; April 1982 (Unclassified, AD-A114 803)

10. "Dangerous Properties of Industrial Materials"; N.I. Sax; Sixth Edition; Van Nostrand Reinhold Company, Inc., New York; 1984.

This page is intentionally blank.

ACKNOWLEDGMENTS

Rohm and Haas gratefully acknowledges the guidance provided by the LTC Donald G. Harrington (USAMMDA), the Contracting Officer's Representative on this contract, throughout the course of this project. His unique perspective and close involvement in the technical aspects of this very challenging project has been invaluable in the overall success of this program.

We wish also to thank Dr. Ronald L. Joiner and his staff at Battelle MREF for their cooperation in the conduct of the in vivo agent studies in support of this contract. Their timely responses and rapid feedback were very important in making proper selections of decon resin candidates for retention in the program.

The spectral reflectance results on the final decon formulations and some of the early candidate systems were provided by the Materials, Fuels and Lubricants Laboratory at BRDEC, Ft. Belvoir, VA. We wish to thank Mr. Jeffrey Duncan and Mr. Robert Benshoff for their expertise and assistance.

This page is intentionally blank.

DISTRIBUTION LIST

1 copy — Commander
US Army Medical Research and Development Command
ATTN.: SCRD-RMI-S
Ft. Detrick, Frederick, MD 21701-5012

5 copies — Commander
US Army Medical Research and Development Command
ATTN.: SGRD-PLE
Ft. Detrick, Frederick, MD 21701-5012

2 copies — Defense Technical Information Center (DTIC)
ATTN.: DTIC-DDAC
Cameron Station
Alexandria, VA 22304-6145

1 copy — Dean
School of Medicine
Uniformed Services University of the
Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814-4799

1 copy — Commandant
Academy of Health Sciences, US Army
ATTN.: AHS-CDM
Ft. Sam Houston, TX 78234-6100

CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved
OMB No 0704-0188

RT SECURITY CLASSIFICATION lassified	1b RESTRICTIVE MARKINGS
RITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION/AVAILABILITY OF REPORT Distribution Limited to U.S. Government Agencies only; administrative/operational use, test and evaluation. Feb 12, 1987
ASSIFICATION/DOWNGRADING SCHEDULE	
RMING ORGANIZATION REPORT NUMBER(S)	5 MONITORING ORGANIZATION REPORT NUMBER(S)
E OF PERFORMING ORGANIZATION n and Haas Company 6b OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
RESS (City, State, and ZIP Code) n and Haas Company ependence Mall West ladelphia, PA 19105	7b. ADDRESS (City, State, and ZIP Code)
E OF FUNDING/SPONSORING ANIZATION U.S. Army Medical rch & Development Command 8b OFFICE SYMBOL (If applicable) SGRD-RMI-S	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-85-C-5200
RESS (City, State, and ZIP Code) t Detrick derick, MD 21701-5012	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 63751A; PROJECT NO. 3M463; TASK NO. BA; WORK UNIT ACCESSION NO. 022

E (Include Security Classification)
Development of a Safe and Effective Skin Decontamination System: Demonstration and Validation (U)

ONAL AUTHOR(S)
. Kopchik, N. Borenstein, D.W. Horsey, J.H. MacDuff, R.B. Steigerwalt, H.H. Miller

PE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
al Report	FROM 7/15/85 TO 1/14/87	1987 February	159

PLEMENTARY NOTATION

COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
.D	GROUP	SUB-GROUP	Chemical Agent; Skin Decontamination Kit; Personnel Equipment
5	20		
7	03		

TRACT (Continue on reverse if necessary and identify by block number)

In this concept exploration/demonstration and validation phase of the sonnel/Casualty Decontamination System Skin Decontamination Kit (PCDS SDK) gram, it was shown that a safe and effective skin decontamination system elopment against chemical warfare (CW) agents can be designed based on AMBERGARD 555 or AMBERGARD XE-556 resin decontaminant developed by Rohm and Haas Company. prototype PCDS SDK developed as part of this contract evolved into a novel soft k design. Each PCDS SDK consists of six applications of decontamination material individual flexible pouches with its own pad for applying, spreading, and removing the decon material. Four thousand prototype PCDS SDK were produced. A Special Process Review recommended that the program proceed to the Full Scale Development se.

TRIBUTION/AVAILABILITY OF ABSTRACT NCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION Unclassified
ME OF RESPONSIBLE INDIVIDUAL rs. Judy Pawlus	22b. TELEPHONE (Include Area Code) 301/663-7325 22c. OFFICE SYMBOL SGRD-RMI-S

m 1473, JUN 86 Previous editions are obsolete. SECURITY CLASSIFICATION OF THIS PAGE